SAJOUS'S ALYTIC CYCLOPEDIA OF ACTICAL MEDICINE

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EIGHTH REVISED EDITION

104 ILLUSTRATIONS

VOLUME NINETEEN

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PREFACE

In accordance with a policy adopted after the publication of the Cyclopedia of Medicine, the Editors and Publishers have prepared a new annual Service Volume for the benefit of the subscribers to the Cyclopedia Experience has amply demonstrated the value of these service volumes as a means of revising and bringing up to date the original contributions that comprise the Cyclopedia. Furthermore, they provide a handy and concise form of post-graduate instruction for busy practitioners, based as they are upon critical reviews of important advances that have taken place in medicine, surgery and the various specialties during any given year It should again be emphasized that in the Service Volume, no attempt is made to prepare a complete abstract of current medical literature. In the preparation of this Service Volume, the effort has been made carefully to appraise the current medical literature of the world, and to give to our subscribers thoughtfully written, complete reviews on subjects that have attained real importance and represent advances in medicine that are outstanding

This Service Volume has been prepared under the direct supervision of the editorial staff of the Cyclopedia Their efforts have been supplemented by those of a large group of well selected contributors Each contributor has been chosen because of his ability and pre-eminence in special fields of work. In this way it is possible to bring to our subscribers reviews that have been prepared with critical judgment and may be depended upon as authoritative

In the discussion of the various topics, a definite policy has been followed for the most part. In the case of the more important subjects an attempt has been made to precede the analysis of the current literature by a brief summary of what may have appeared on the subject in earlier Service Volumes. In this way, a certain cumulative value is added to the present volume. It will be noted that in all the subjects discussed, especial attention has been given to diagnosis and treatment, although other aspects of importance have not been neglected. It is felt that this plan materially adds to the practical value of the work

As in former Service Volumes, the material has been divided into the main divisions of medicine. Approximately one-third of the volume is given to internal medicine another third devoted to general surgery, and the remaining third subdivided among the various specialties, including ophthalmology, otorhinolaryngology, pediatrics, clinical pathology, general therapeutics, devoted largely to the discussion of the newer drugs, physical therapy and its various branches, and finally dietotherapy

Under medicine will be found the generally recognized subdivisions of internal medicine such as allergy, rheumatoid conditions, diseases of the cardiovascular system, endocrinology, hematology, renal diseases, metabolic disorders, diseases of the respiratory tract, gastroenterology, and an unusually extensive section on neurology and psychiatry. Dermatology, syphilis, and diseases of the teeth are also included in the medical section. Because of the exceptionally large amount of outstanding work that has been done in cardiology, endocrinology and metabolic iv PREFACE

disorders, these sections are deserving of special note. Under metabolic disorders will be found a complete discussion of the newer forms of insulin and its uses, and the latest advances in vitamin disorders and therapy

The section on surgery opens with a compendious review of abdominal surgery. The various forms of anesthesia are next discussed. There then follow such timely topics as surgery of the sympathetic nervous system, including the surgical treatment of essential hypertension, and endoscopy in its various important aspects. The subjects of cancer, orthopedic, thoracic, thyroid and vascular surgery are all adequately dealt with. Extensive sections are devoted to the major subjects of urology, x-ray and radium, particularly from a therapeutic standpoint. A separate section is given over to the much discussed injection treatment of hernia. Gynecology and obstetrics are included under the general heading of surgery with almost a hundred pages devoted to a comprehensive review of these important subjects.

The Editors believe that this Service Volume represents the most complete, practical, up-to-date review of progress in medicine and surgery that has ever been offered the subscribers to the Cyclopedia of Medicine

A volume such as this has been made possible through the enthusiastic support and tireless efforts of the Associate Editors and many contributors to whom the Editor expresses his sincere thanks. Dr. Edward L. Bortz, who planned and directed the preparation of this volume, is deserving of all the credit for its success. To him also goes the grateful appreciation of the Editor for his unfailing help and wise counsel. To Mr. George B. Johnson and Dr. Frederick C. Smith thanks are due for seeing the volume through the press and preparation of the complete index. The Publishers are to be congratulated upon the generous way in which they have enlarged the size and scope of this Service Volume and for their liberality in greatly increasing the number of illustrations.

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The Cyclopedia of Medicine

Revision Service - 1938

MEDICINE

Edited by George Morris Piersol, BS, MD, and Edward L Bortz, AB, MD

ALLERGY

By Harry Bond Wilmer, M D, and Merle Middour Miller, B S, M D

ASTHMA

Introduction—Therapeutic measures in bronchial asthma have to be employed in two stages of the disease (1) In an acute attack designated by some as status asthmaticus Varying degrees of the paroxysm are identified by this term (2) During a remission of symptoms at which time we use prophylactic means to prevent subsequent exacerbations Leon Unger has shown in a series of 207 cases that results are better in the extrinsic group of asthmatics than in the intimsic or so-called bacterial classification The former consists of those patients in whom there is some demonstrable sensitivity to some environmental substance whether it be ingested, inhaled or encountered by contact only group is made up of those patients whose asthma is usually a symptom of some underlying medical condition, most often a focus of infection. At times we are confronted with a mixed type which may either simplify or complicate the issue

Principles of Therapy—In the extrinsic group one can readily apply the

two cardinal principles of allergic therapy, i e, elimination and hyposensitization If it is impossible to remove the offending substance or to change one's surroundings, then it is hoped that desensitization can be accomplished hereditary history of allergy is in many cases elicited from patients in the extrinsic class, or they themselves have had previous personal allergic manifestations At times we have discovered an allergy in a patient by carefully examining symptoms and sensitivity in his children Knowing them to be allergic, we have tested the patient, and found him to be hypersensitive F M Rackemann found approximately the same results as Unger ten years later has shown in his group that about 20 per cent are so-called "cures," 50 per cent are improved slightly moderately, or markedly, and 20 to 30 per cent show no results. In all cases there is usually a tendency to relapse, and for this reason all allergic individuals should be under supervision for life

A few salient points in the treatment of the attack are the following

(1)

Epinephrine—In doses of 5 to 15 minims (03 to 1 cc) epinephrine (adrenalm) 1 1000 dilution is the drug of choice and may be repeated at frequent intervals. It is most efficacious at times, but is often impotent in a chronic asthmatic It is not habit-forming and usually no permanent damage is encountered from its use. The use of this drug at many times is contraindicated in patients with marked hypertension, but there are cases in which we have not noted an appreciable rise in blood pressure We therefore feel that at times, if used cautiously, it is relatively safe in the hypertensive Injections of epinephrine must be administered as early in the attack as possible and sometimes given at regular intervals, i e, every two or three hours for 24 to 48 hours, with the hope of possibly building up an "adrenalin reserve" and breaking the asthmatic cycle. It may be given more frequently if the occasion arises

I B Gracser and \ H Rowe have obtained beneficial results in the treatment of bronchial asthma by the inhalation of a solution of epinephrine, 1 100 For the spray, an atomizer should be used which vaporizes the solution to a degree sufficiently fine that the particles will be disseminated to all parts of the lungs. A glass atomizer that delivers an even vapor-like spray has been perfected. The use of an inferior atomizer may produce unpleasant and annoving dryness of the throat and, at times, gastrointestinal upsets from contact of the strong solution with the various mucous membrane surfaces. The dosage varies with the patient and at the beginning it is a "trial and error" method Caution must be observed, but the only untoward symptoms noted have been severe headaches from prolonged use and a dryness of the throat Only rarely have we noted any constitutional reactions It is well to allow several minutes to elapse between deep inhalations. In a great many instances the use of the 1 100 solution by inhalation has supplanted the hypodermic injections of the 1 1000 solution. As a prophylactic, it is suggested that repeated inhalations during the free period of the day may prevent recurrent attacks, or mitigate the severity of any paroxysm that might develop

Ephedrin—Ephedrin may be given by mouth, but it is efficacious in mild cases only The usual dose is 3/8 to 3/4 grain (00243 to 00486 Gm) Often untoward nervous symptoms develop from the prolonged use of ephedrin salts Synthetic ephedrin preparations, propadrin, etc., are of some benefit in mild cases and these usually do not give the unpleasant side effects we often get from ephedrin J H Murphy reports that he has treated a group of patients with propadrin, and believes the dosage of this preparation about equivalent with that of the ephedrin He also feels that this preparation can be used over a longer period of time without any significant reactions. We believe that propadrin produces results in some cases but in our short series we have found that it is necessary to give larger doses than those usually found effectual when using ephedrin

Morphine—Morphine should not be given in acute asthma unless epinephrine has failed, and when given, morphine should be tried very cautiously, at first used in small doses. Many asthmatics have an idiosyncrasy to this and other opiates. Often morphine gives the rest needed by an asthmatic and may have to be used Pantopan and dilaudid can be used instead of morphine, and good results have been obtained with these two derivatives.

ALLERGY 3

Atropine—Atropine gives bronchial relaxation and dilatation but at times has an unpleasant drying effect on the secretions and renders the tenacious mucus in an asthmatic chest even more mucilaginous. It is often well to use it with the first dose of morphine. Subsequent or alternate doses of the opiate can be given without the atropine.

Glucose-Bray, Black and others have used glucose intravenously in acute attacks in doses of 20 to 50 cc of a 50 per cent solution. It may be given every four to six hours and then once or twice daily until the patient is well able to take sufficient carbohydrate by mouth In these cases the carbohydrate metabolism perhaps is normal, but these patients, often cachectic and undernourished, are in need of this form of concentrated nourishment. If the patient is dehvdrated, a five to ten per cent solution in larger doses may be given slowly over a longer period of time if indicated Some workers have been using a 50 per cent sucrose solution in doses of 50 cc. This probably has a more prolonged effect, and is possibly more dehydrating, and seems to give better results L N Gay, Baltimore, recommends this form of carbohydrate intravenously, and has treated many cases with this preparation

Treatment of Refractory Cases-

A certain percentage of patients in status asthmaticus do not respond to the usual dosage of epinephrine, ephedrin and morphia. These individuals present a case of extreme misery and suffering I. S. Kahn¹ presents 16 cases, all desperately ill, and in all of whom hypodermic injections of *epinephrine* in the usual doses were of absolutely no effect in relieving the asthmatic paroxsym. He believes that when this drug in doses of the usual size has failed, its further indication and efficacy can better and more safely be determined, not by in-

creasing the dose given hypodermically, but by proceeding cautiously intravenously. He suggests the use of a 1.1000 dilution in doses of two to four minims (015 to 025 cc) using a tuberculin syringe and a 26 gauge needle He states that, even if given in such small doses and slowly, this is an extremely shocking measure; terrific pallor, tremor, sweating, headache, heart pounding, and at times terrific nausea and vomiting occur almost instantly He has never seen a patient who has failed to develop either some or all of these symptoms. It is felt that some of these untoward reactions can be avoided or reduced by using a 1.10,000 dilution

If some relief is obtained in these most severe cases, subsequently the patients can be maintained on the usual hypodermic doses. It seems necessary to break the asthmatic cycle, and to produce some relaxation. We have found in cases in which it was necessary to give epinephrine intravenously, that it is well to proceed by the following method give from two to four minims (0.15 to 0.25 cc) in $\frac{1}{2}$ to $\frac{2}{3}$ oz (10 to 20 cc) of normal saline solution. This is given in a large syringe with a 26 or 27 gauge needle, and given quite slowly procedure we have found, at times diminishes the marked symptoms and signs following the administration of this drug intravenously. Also, we feel that the administration of epinephine by the intravenous method should be used only in extreme cases, very cautiously, and in minute doses

If these refractory cases do not respond to intravenous epinephrine, Kahn reports beneficial results from the use of a thoroughly mixed combination of anesthesia ether and olive oil. He states that the best dosage is from five to seven ounces of the mixture. We

also feel that the smaller dosage should be tried first C K Maytum² has also reported results from this procedure

In a series of sixteen cases treated by Kahn there were no deaths, and relief was usually noted in 6 to 12 hours He feels that a great many of the methods employed are of no avail in patients with refractory asthma except (1) hypodernic epinephrine, (2) intravenous epinephrine, (3) rectal anesthesia, and (4) morphia if absolutely necessary. The oxygen tent has helped some cases who were markedly evanotic At times this procedure is very distressing to the patient and its use must be discontinued The barbiturates must be used cautiously, as they are generally quite ineffectual, and if given we advise administration by mouth only

Bronchoscopy has been resorted to m intractable asthma, but in status asthmaticus of the extreme type this procedure is most difficult and often ineffectual. One case in which we have used it suffered quite severely after his treatment.

In discussing Kahn's work, B. G. Lifron, New Orleans, reported that he has used aminophyllin intravenously with some success in cases of asthma which are 'adrenalin-fast'. About 33 per cent of his patients responded favorably to this drug. We have used aminophyllin by mouth in a great many patients with bronchial asthma, who are not in status asthmaticus. It seems to be beneficial, especially in those who have some myocardial damage and poor coronary circulation.

In patients with cyanosis the oxygen tent is often tried. At times, as we have quoted, the patient becomes more distressed and respirations are more difficult. Baroch was the first to report on the use of a combination of *helium and* oxygen. This combination is quite effectual if the helium is available. Several workers have seen beneficial and quite outstanding relief with this combination

Iodized Oil—L. H. Criep and J. H Hampsey,³ publish for the first time a complete report of the opinions of a large group of allergists concerning the use of iodized oil The first reports of the use of the preparation in bronchial asthma reached the literature in 1932, and in the ensuing five years many men have had experience with this preparation Taylor, Fink and Anderson, R M Balyeat and L. E Seyler⁴ and so on through to the present, Dr Criep's review is the most comprehensive to date on this method of treatment

Iodized oil can be administered in several different ways, ie, (1) the intra-nasal catheter, (2) gravity method, which is accomplished by pulling the tongue forward and allowing the oil to run down. (3) intra-tracheal instillation by a laryngeal syringe, (this technic is described by R. M. Balveat, L. E. Seyler, and H. A. Shoemaker, and (4) bronchoscopic application, which some workers contend is by far the best method. For practical and routine use it is telt that instillation by the laryngeal syringe is the most desirable means of administration.

I ntoward reactions observed from the use of iodized oil are as follows (1) Iodine sensitivity and iodism, Balyeat reports as a possibility. We have had one case in which quite marked idema and inflammation of the respiratory mucosa followed the instillation of the oil. Subsequently this patient was proven highly sensitive to iodine preparations. W. Anderson⁶ observed severe iodism in eight cases. (2) Convulsive cough often follows the introduction and there is a possibility of massive collapse of the lung or a lobular atelectasis. (3)

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Criep encountered the following distressing symptoms, severe dyspnoea, evanosis, and circulatory failure from which the patients recovered Plehn reported one case of traumatic bronchiectasis following a prolonged convulsive (4) Pneumoma developed in eight of Anderson's cases, all but one recovered Other workers report oil in the lungs months to years after the instillation (5) Allergic reactions characterized by urticaria, asthma. arthritis and fever have been referred to by different observers A sensitivity to the oil used as a vehicle for the iodine is thought to be a factor in some cases

Fatal termination to complications resulting from the use of the instillation of iodized oil is not rare, and Criep feels that all the disadvantages and possible untoward reactions noted above should be carefully weighed before treatment of this type is instituted. There are times when this mode of therapeusis in intractable asthma is possibly indicated in a selected group. At present allergists in general are not very enthusiastic about the use of iodized oil and it is quite significant to find that only about one third of the physicians who have tried this method are still using it, and these only as an adjunct in some cases Benefit obtained from this preparation is usually only temporary, and results are due only to the mechanical effect of the oil on the bronchial tree. It has never been proven that any clinical desensitization is accomplished by its use. A small percentage of a well selected group of respiratory cases of bronchial asthma may get temporary relief. Anything new that will give chronic asthmatics rehef, whether temporary or permanent, arouses interest in general, and we are all indebted to Dr. Criep for his careful and complete compilation and summarization of a mode of therapy that has

aroused the attention of the medical profession.

Potassium iodide in doses of 5 to 15 grains (0.3 to 1 Gm) three times daily is probably the best alterative and liberator of bronchial secretion available at present. Some allergic individuals cannot tolerate therapeutic doses, but this preparation is worth a trial in all asthmatics, especially of the intrinsic or mixed type

Other iodine products have been used in treatment. Although comparatively rare, there are allergic individuals who have hyperthyroidism of varying degrees. If this condition is mild, and surgery is not indicated from the standpoint of a thyrotovicosis, then Lugol's solution may be used in doses of 10 to 20 minims (0.6 to 1.3 cc.) daily. A basal metabolism should always be done before this preparation is given

Rest—B. A Credille⁷ stresses the importance of rest in the treatment of allergic diseases. Fatigue and exhaustion are very vital secondary factors, and, as has been found, often the most important mechanism in precipitating an attack. He believes that an allergic individual has a definite fatigue threshold. When this is lowered, the patient is more likely to have an attack. Prolonged rest is a most valuable adjunct in the treatment of asthma, asthmatic bronchitis, and the like. This is especially true of the "high strung," nervous type of patient.

A hospital is the ideal place for complete relaxation and rest. It has been the writer's experience in many cases that hospitalization for se was enough to give a patient complete relict, without any medication, hyposensitization, etc. Improvement practically always follows continued rest, both physical and mental. Complete rest is the first and

most important part of any acute asthmatic regimen

Piness once made the statement that if the individual in status asthmaticus is given complete mental and physical rest, plus fluids, he will usually come out of the attack in good condition. As we have previously stated, there are many adjuncts in the treatment of bronchial asthma, but first and most important is complete rest.

X-ray Therapy—C K. Maytum and E T Leddy's report the treatment of 23 asthmatics with x-ray therapy. These patients were all refractory to other methods of treatment. The series of cases included all types of asthma and was not a selective group.

Irradiation of the mediastinum through two paravertebral fields seemed to give less gastro-intestinal reaction than the anterior-posterior cross-fire. If no contraindication exists, and the patient is able to be prone without discomfort, the treatment is given over the mediastinum from the rear, ascending to the following formula.

| K V | 135 |
|----------|------------------|
| Filter | 6 mm AL |
| Distance | 40 cm |
| Time | 22 to 26 minutes |

One treatment usually suffices for a time, but may be repeated at intervals if absolutely necessary

The mechanism of relief is not known, but as Desjardins has reported, is probably due to a decrease in the secretory power of the mucous glands in the trachea, and probably a liberation of antibodies due to the destruction of leukocytes, and also a stimulating effect on the production of eosinophiles. These workers believe that x-ray therapy is a definite adjunct in the treatment of asthma, and its most important benefit is in its ability to interrupt the cycle of paroxysmal attacks.

SURGERY AND ANESTHESIA

R Andre and R C Grove report a survey of a group of 204 allergic patients who had nose and throat surgery under general anesthesia. Their findings are most important, as the allergist and rhinolaryngologist are confronted by two problems (1) when to operate on an allergic patient, and (2) what type anesthesia to use It has been found from observation of this series that general anesthesia is safe in allergic patients It may even be used in the severe asthmatic if the case is carefully selected and prepared A method which employs small amounts of anesthetic with carbon dioxide and oxygen hyperventilation is found to be the one of choice In this group pulmonary complications were noticeably absent

H Schenck, in discussing this paper, states that from the conclusions in this study, it would seem that general anesthesia is as safe in allergic patients as in others. He cautions that the anesthetic and operation should not be trusted to average operators and anesthetists. It is most necessary that all patients be subjected to painstaking preoperative treatment and the proper attention must be given to basal anesthesia and hyperventilation at the close of the operation Avertin has been used successfully by the above workers and has been found satisfactory by others. This anesthetic has also been tried in intractable bronchial asthina

The authors of this section had a patient in severe status asthmaticus. During this distressing period he developed acute appendicutis and it was necessary to operate **Ether** anesthesia was used and during the anesthesia the patient was free of severe asthma for the first time in ten days. Following the operation he was much more easily

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controlled by hypodermic epinephrine than previously. As a great many physicians who have seen a large number of patients in status asthmaticus can attest, during ether anesthesia the patient is markedly relieved, and, unless there are other contraindications, ether is often the anesthesia of choice in certain cases of asthma

Local Anesthesia

Many operations on the upper respiratory tract in allergic patients can and should be done under local anesthesia This again calls for selectivity of cases as to temperament and physical condi-Schenck advises the use of local anesthesia in the radical operations of Caldwell-Luc and Ferris-Smith This is suggested because it minimizes shock and gives the operator a dry field of operation. A great deal may be said for both types of anesthesia, but the importance of the correct selection of cases for each form must again be emphasized Whether the operation is done under local or general anesthesia, the preoperative care and postoperative management assume rôles of extreme importance

CARBOHYDRATE METABOLISM

Carbohydrate metabolism we believe influences the state of an allergic individual. We have been investigating and observing the variations in metabolism in the allergic patient for the past four years, and estimation of the glucose tolerance has been done on more than 1100 patients. An outline of therapy has been presented which takes into consideration the allergic individual's metabolic and endocrine background. First, it is the usual procedure to eliminate all offending allergenic substances.

Secondly, hyposensitization for the protems which cannot be removed from the patient's environment After a glucose tolerance test has been done, we can approximately determine whether a patient metabolizes sugar rapidly or not If his carbohydrate mechanism is of the appropriate type, we then supplement his usual diet with one tablespoon of dextrose in fruit juice three times daily. This is given at the times in the day when the blood sugar is thought to be at its lowest level, i.e., at the end of the morning, late afternoon, and on retiring. This preparation clinically has no specific effect on allergic state per se, but does seem to be a supplementary form of therapy that is highly efficacious, especially in those who are thin, frail, cachetic, and suffering from hyponutrition

H B Wilmer and M M Miller⁹ presented evidence of an altered carbohydrate mechanism in allergic individuals In 633 glucose tolerance determinations done on 513 allergic individuals, only one patient was found to be diabetic with sugar in the urine. This is an incidence of 002 per cent in comparison to 17 per cent in normal persons. Allergic individuals often manifest all the evidences of hypoadrenia, low blood pressure, asthenia, hypoglycemia, soft small pulse, and definite vasomotor instability, but there is no evidence that the adrenals alone are at fault

ENDOCRINE PREPARATIONS IN THE TREATMENT OF ALLERGIC DISEASES

Hypofunction of the suprarenals is at least part of the picture in allergic disease. With this in mind, we have been actively treating patients with supplementary glandular therapy during the past three years. First we used cortical hormone, processed by the Swingle-

Pfiffner method. The results, at times most outstanding and spectacular, were by and large far from satisfactory and often disappointing. Tabulations of our findings in this form of treatment were presented, and showed 13 per cent beneficial results in refractory cases by H. B. Wilmer and M. M. Miller¹⁰. Since that time we have been using extracts of the suprarenal gland by mouth. Two commercial products have been found most satisfactory, *suprarenal concentrate* and *glycortal*. The dosage of each is four to eight capsules or tablets daily.

Rogoff and Stuart, Harrop and Swingle, Pfiffner and Parkins, among others, have advocated the use of **sodium chloride** in adrenalectomized animals as an adjunct in maintaining life. Salt has been added as a supplementary means in patients with symptoms simulating a profound adrenia

We do not believe that the use of adrenal extracts of the type available at the present time, and the addition of glucose and sodium chloride have any marked specific effect on the symptomatology of allergic disease, but a definite, progressive and gradual increase in weight in these asthenic individuals was noted. This corresponds with the findings of Hoskins. Also the patients' general resistance scemed to improve, and a marked feeling of well being was ob-The use of adrenal extracts, sugar, and sodium chloride does not replace the usual extract methods of allergic therapy, but the above named preparations are basic adjuncts in our armamentarium. It is believed that they help reinforce the primary background of endocrine and nervous stability that is so often lacking in the allergic individual At present, if an allergic patient manifests the clinical symptoms of hypoadrenia, no matter whether this state

may be due to a primary hypersensitive background, or the result of long standing debilitating illness, it is well to supplement the usual therapeutic means with a whole gland adrenal preparation

Endocrine therapy is often of extreme importance, especially in patients at the *menopause*. Preparations containing *female sex hormones* are often indicated in cases with complications associated with menses and the menopause. We have used *progynon B* in doses varying from 500 to 2000 rat units at intervals of four to five days, beginning about a week after the last period and continuing to the next. After cessation of menstruation, the dose is given at the same interval, and the amount depends on continued indication or untoward symptoms developing

Thyroid extract has proven a valuable adjunct in cases where there is clinical evidence of hypothyroidism or a low basal metabolic rate, or both A combination of thyroid extract and suprarenal concentrate has been highly efficacious in some of our cases

Investigations of all systems of the body have thrown no light on the true chologic background of allergic disease. This fundamental condition, from which allergy inevitably results, must be found before there is any marked advance in therapy. In the opposing action or synergistic functional activity of any one or group of glands may be found the answer. It is hoped that future investigation may reveal the exact mechanism

HAY FEVER

Treatment—A Vander Veer¹¹ reports a study of the relative ments of the seasonal and perennial treatment of hay fever At present there

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15 a great deal of controversy among allergists as to the better method This article dealt with observations on an average of 430 patients annually questionnaire was sent to each patient who alone evaluated the results obtained According to the chart published in the résumé, it was shown that the perennial results were uniformly better by eight to ten per cent than the seasonal This is according to statistics, but the human equation must be brought into the picture. It is much easier to persuade a patient with complete relief to continue throughout the year than one who has been refractory to the seasonal injections. This factor may tend to place more of the satisfactory cases in the perennial group

There are two disadvantages in the perennial treatment. Many patients forget to take the injections, and if an interval of five weeks has elapsed, the risk of constitutional reaction is increased. There is always the possibility of a patient becoming saturated and into such a state that very small injections will give a constitutional reaction.

In general, the problem is best solved by choosing the right method for each individual patient, depending on temperament, sensitivity, and previous results obtained. The pre-seasonal and coseasonal methods of treatment are quite necessary in many cases, but under ideal conditions and when there are no untoward symptoms, it is felt by a great many allergists that the perennial treatment is, by and large, the method of choice. Vander, Veer, considers, that perennial treatment is more likely to produce a permanent so-called "cure" eventually than the other methods.

Rapid Hyposensitization — This method of making a patient less sensitive has been employed by us for different allergenic substances. Four cases of un-

complicated epidermal sensitivities were treated in this manner: Each patient was hospitalized and given an injection hypodermically of the offending atopen every hour until he had reached the limit of tolerance. The dilution of the first dose was 1 100,000, and the first dose was 0.1 cc. The maximum dose reached was 0.5 cc. of a 1 100 dilution. This hyposensitization was accomplished in 48 hours in each case. On subsequent contact no symptoms were elicited. It is important to remember that these patients were entirely removed from contact with the substance to which they were sensitive during the period of hyposensitization

Nincteen cases of pollen asthma were treated in the same manner. A complete course of pollen injections was given at intervals of one to two hours first dilution given was 1 10,000, and the first dose 0.1 cc. The maximum dose given was 0.5 cc of a 1.500 dilution Sixteen of the 19 cases were completely hyposensuized and remained so during the rest of the season. Some have been put on perchinal treatment while others we have allowed to go until the One case became very next season toxic during the period of treatment and this procedure had to be discontinued. Two of the patients had no rehef whatever There were no more constitutional reactions encountered than we usually get in the pre-seasonal method. In only one case was it neces sary to stop the injections

Precautions observed were (1) It any local reaction was observed, the same dose was repeated or the interval lengthened to two hours (2) The patient was entirely removed from contact with the offending substance (3). Four of the patients were put in airconditioned or allergen-free rooms (4). Patients were hospitalized and kept in

bed under constant supervision during the period of hyposensitization (5) Injections should be stopped if any constitutional reactions develop

This is only a preliminary report, but we believe that we have enough evidence to show that this method of treatment has a place, especially in this era of allergen-free rooms. It is possible that if hyposensitization is accomplished it is not as lasting as the longer interval method

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ARTHRITIS AND RHEUMATOID CONDITIONS

By RALPH PEMBERTON, MS, MD, and C W Scull, MS, PhD

Introduction — Before considering the contributions to the literature during 1937 a brief review of some of the more important considerations appearing within the past few years should be mentioned. The problems of diagnosis and treatment of rheumatoid diseases may at times appear to be made more complex rather than simpler by the deluge of papers appearing in the medical journals. However, there have appeared during the past few years several series of discussions which clarify these questions.

Pathogenesis — Fecal Flora — The attention which has been directed toward the gastromtestinal tract as a possible source of toxemia in arthritis and the occasional use of stool cultures as a means of detecting the presence of alleged etiological agents gives relevance to the contribution of S H Stabler and R Pemberton⁸ on the intestinal bacteria in *chronic arthritis* These investigations examined the stools of arthrities and

normals with respect to the total numbers of viable bacteria per gram of feces, the kind and approximate numbers of groups of organisms identified as coliform, lactobacilli, gram-positive cocci, aerobic and microaerobic streptococci and aerobic No group is characteristically present in the stools of either group of arthritics or of normals. The total numher of organisms is higher in the feces of atrophic and hypertrophic patients than in those of normals. The fact that strains of streptococci are present in normals as well as arthritics indicates the impropriety of attaching specific significance to the recovery of these organisms from the feces of such patients

Observations upon the possible influence of certain dietetic measures with respect to the fecal flora do not reveal consistent departures from the established kinds and numbers of bacteria present. It is concluded that dietetics do not alone determine the numbers of intestinal bacteria and that the rôle of dietetics is

not confined to an influence upon the flora in the intestinal tract.

Pathology-Liver Function - The importance of a study of liver function, particularly in atrophic (rheumatoid or infectious) arthritis is suggested by W. B. Rawls, S. Weiss, and V L Collins 9 The incidence of liver dysfunction among 100 patients of atrophic arthritis is evident by an abnormal rate of excretion of Azorubin S in 55 subjects. Furthermore evidence of disturbed function tends to parallel the degree of clinical severity of the rheumatic condition The authors suggest that liver dysfunction may influence the decreased glucose tolerance noted among this group of patients as well as the disturbed levels of serum proteins. It is evident that measures designed to modify the consequences of decreased hepatic function should be employed These include the provision of optimal supplies of materials in the diet and removal of sources of toxaemia

Differential Diagnosis—Among the outstanding series of articles dealing with differential diagnosis in rheumatorid diseases, brief mention should be made of the symposium on the topic by the American Association for the Study and Control of Rheumatic Diseases

R H Boots points out that atrophic arthritis in that the former shows positive agglutinins for hemolytic streptococci in more than 50 per cent of cases, an increased sedimentation rate, often a slight leukocytosis, whereas the latter exhibits slight if any changes in this direction. The former shows early evidence of osteoporosis, perfarticular swelling and foint effusion, and finally narrowing of the joint space, bone destruction, ankylosis, and marked muscular wasting, while the latter, according to Boots, shows no osteoporosis, does show hipping

at joint margins and finally osteophytes, without marked muscular wasting

I. L Miller differentiating atrophic spondylitis from hypertrophic spondylitis believes that the former begins in the small articulations of the spine as an inflammatory process, which according to this author, also involves the nerve. Coincident with these processes osteoporosis of the vertebrae occurs changes are followed by ankylosis and by ossification of the intervertebral ligaments, occasionally with extension of the spongiosa of the vertebrae through the discs. Infectious factors appear to be etiologic. On the other hand, hypertrophic lesions in the spine begin with decreased resiliency and thinning of vertebral discs, followed by greater strains upon the intervertebral ligaments These enter the periosteum of the vertebrae adjacent to the vertebral rim, and the resultant irritation of the periosteum leads to the formation of osteophytes along the course of attachment. Degenerative factors appear to be etiologic Differentiation of these two types in late stages is easily made upon the basis of roentgenographic features, the osteoporosis, round smooth bamboo stick appearance of the spine and calcified intervertebral ligaments in the atrophic variety and the lack of osteoporosis and the irregular osteophyte formations in the hypertropluc type

R A kinsella points out the factors differentiating the umatic texes from Still's disease acute atrophic arthritis arthritis incident to acute bacteria about the joints acute your, and early phases of aonococcal rheumatism. The principal criteria for a diagnosis of sheumatic texes center around the fact that it is associated with cardiac lesions while the other members lack this symptom. Still's disease is characterized by a more insidious onset, a persistence of joint involvement,

a greater tendency toward an involvement of lymph nodes and spleen, than occurs in rheumatic fever and is further distinguished by a lack of cardiac involvement. Similar considerations apply to the diagnosis of acute atrophic arthritis of the young adult Severe infections may simulate rheumatic fever but lack the periodicity of attack and the persistence of cardiac lesions gonococcal arthritis may also resemble rheumatic fever but can be distinguished by the presence of associated genitourmary infection and the infrequency of Gout and acute stages heart disease of hypertrophic arthritis occur in later life and are not often to be confused with rheumatic fever

W C Campbell indicates that uncomplicated traumatic arthritis exists as a definite entity only in the young and is usually monoarticular The pathologic picture is variable but in the main presents one of localized hypertrophic arthritis arising as a result of constant nutation incidental to the functional activity of a joint which by then has become more or less meongruous. There may be local osteoporosis with mottling at the end of the bone from a vasomotor This is to be distinguished from the atrophy of disuse, which presents evidence of extension to the cortex The chief diagnostic factor is the history of muny followed shortly by the appearance of symptoms. I rauma may be a determining factor in the localization of other types of joint disease injuicd tissues constitute a locus minoris resistentia, more easily subject to influence from noxic agencies Mechanical mjury to joints already affected by some form of arthritis may be more serious than that of a similar injury to a normal joint, and furthermore the sequelae are often more disabling than the original injury

C H. Slocumb regards persarticular fibrositis as likely to simulate arthritis, although intramuscular fibrositis is not often mistaken for it The final diagnosis depends upon the fact that fibrositis occurs without interference with the original integrity of the joint per se Fibrositis is distinguished by clinical evidence that articular tenderness and marked muscular atrophy are both lacking Stiffness is largely subjective, hydrops from synovial reaction is absent, ordinary motion is usually painless, and indeed mobility may be increased as a result of voluntary motion, remissions are frequent, systemic manifestations are usually absent or minimal and loss of weight is often slight Periarticular fibrositis presents little if any x-1av evidence of intra-articular change The sedimentation rate is slightly, if at all, accelerated and there is a lesser tendency to anemia. The systemic manifestations are on the whole distinctly less than in arthritis and this provides sufficient grounds for differentiation

F D Dickson points out considerations required to differentiate tuberculous arthritis from other varieties Tuberculous arthritis tends to be mono-articular and to occur in early life. The history usually reveals tuberculous exposure and an insidious onset Pain develops relatively late in the course of the disease but the changes are chronically progressive. The relative incidence of the sites of affection is indicated in a series of 158 cases in which involvement occurred in the spine in 62, in the hip in 41, in the knee in 25, in the ankle in 11, in the wrist in ten, in the sacroiliac in six, in shoulders in two, in elbow in one Constitutional symptoms are frequently absent Limitation of motion is slight and the swelling is boggy, unlike that presented by the effusions and marked muscle atrophy which marks atrophic arthritis The appearance of lesions may be similar to that of syphilitic synoritis. Late x-ray studies show thinning of cortex, destruction or thinning of cartilage, decalcification of bone ends, lack of new bone formation, presence of a focus of bone destruction in epiphysis, which tends to involve the neighboring joint Multiple articular arthritis is rare and is distinguished from other forms in that it tends to be assymmetrical. Tuberculous arthritis of Poncet differs from atrophic arthritis only because of evidence of tuberculous infection in the former

P S Hench re-emphasizes the fact that gout occurs chiefly in males (98 per cent of cases) and occurs most frequently after the age of 40 years Gout may be distinguished from atrophic arthritis by the fact that the onset of pain is rapid and reaches a maximum in two days Complete symptomatic remissions lasting for months often occur disease progresses the attacks become more frequent and the joint changes become chronically progressive The swelling is often hot, bluish red, and is assymmetrical Gouty arthritis is prone to be precipitated by dietary indiscretion, exposure, trauma, and occasionally develops during postoperative periods, during application of ketogenic diets, insulin and iron therapy. Coincident occurrence of nephritis, renal calculus, polycythemia and leucopema are suggestive, and the appearance of uratic tophi is pathogno-Areas of hone erosion if present are likely to be larger in size and more irregular in shape than the corresponding features in atrophic arthritis. Hyperuricenna is not a consistent feature but when present is highly significant

W J Kerr cites some of the less common conditions which may be mistaken for arthritic disorders. Syphilis the history, presence of other syphilitic lesions, and serologic tests establish the diagnosis. The articular lesions include

not only Charcot's type which may present bizarre features of atrophic and hypertrophic character but also less distinctive features, such as periostitis or fusiform swelling of fingers. Hemophilia with hemarthrosis due to bleeding in the synovial membrane, may lead to progressive articular change, simulating hypertrophic arthritis but is easily distinguished by the history and delayed clotting time. Scorbutic changes in the joint are suggestive of atrothic arthritis but the capillary fragility, the generalized tendency toward hemorrhage, along with a graphic response to vitamin C, easily separate this entity. Beri-beri of the dry type showing pain and weakness in the extremities, with parasthesias, muscular tenderness, and of the wet type with edema masking nutritional wasting, may simulate part of the symptoms evident in atrophic arthritis but the history of dietary deficiency and response to nutritional factors establish the diagnosis Rukets in children may, because of swelling in the ends of bones, grossly simulate, in its early stages, atrophic arthritis However, irregularity of epiphysial lines evident in roentgenograms, along with the history and general clinical picture, should leave little room for serious doubt as to diagnosis. Raynaud's disease and scleroderma are frequently associated in the late stages with hone changes like those seen in legrons and with gross joint changes. These changes appear to follow the altered blood supply. Leprosy leads to marked alterations in the bones and joints but the coincidence of lesions of legrosy in other tissues usually establishes the diagnosis by exclusion. Frythralgia may be associated with joint pathology arising as a resultant of the vascular and nervous derangement. Fixation from disuse and contractures may eventually appear Peripheral neuritis occurring as a result of a variety of

intoxications may mimic arthritic pains. Both diabetes and primary anemia may cause sensory symptoms of articular disease Periarteritis, Paget's disease, intermittent claudication, may lead to sensory symptoms. The pain of osteomyelitis, herpes zoster, von Recklinghausen's disease, psychogenic and referred visceral pain may also mimic the pain of arthritis.

Tests—An excellent summary of tests used in the diagnosis of rheumatoid arthritis is presented by C L Short, L Dienes, and W Bauer, who compared the results obtained in the measurement of the sedimentation rate of the erythrocytes, the Arneth-Schilling count, the Vernes resorcinol reaction and the agglutinin tities for various types of streptococci in a group of selected atrophic arthritics. These tests are more or less widely used as diagnostic "criteria and objective measuring sticks" in the evaluation of the activity or atrophic arthritis, although no one of these tests is wholly specific for theumatoid disease alone

It is widely recognized that the rate of settling of the red cells is markedly increased in atrophic arthritis and also accelerated in theumatic fever, gonortheal atthitis, acute gout, most intectious diseases in malignancy, hepatic jaundice, pregnancy and non-infectious conditions associated with extensive tissue destruc-Thus the reaction is obviously non-specific. Inasmuch as the rate is less rapid in hypertrophic arthritis, myositis, filmositis, sciatica and lumbago, it may be used as a guide in the differential diagnosis of rheumatoid diseases which presents only a few objective signs return toward a normal rate in a case of rheumatoid arthritis is regarded as a favorable prognostic sign

The authors recommend the procedure of M D Rourke and A C Ernstene³

as the most useful modification of the In this procedure sedimentation test heparin is used as an anticoagulant and venous stasis is avoided during blood collection The rate of settling is measured in terms of the millimeter drop per minute at the time of the most rapid falling. This value is corrected to a standard hematocrit volume The corrected value so obtained eliminates the influence of anemia per se The extent of correlation with the clinical condition of the patient is precise in 92 per cent of the cases It is therefore recommended as a convenient and accurate measuring stick for the diagnosis of atrophic arthritis and the degree of its activity

The presence of abnormally high numbers of young polymorphonuclear leukocytes has also been noted in atrophic arthritis and in other infectious and non-The authors use infectious conditions a simplified Arneth method Band forms, juveniles and invelocytes are considered together and the percentage of polymorphonuclears is estimated. A count of young cells exceeding eight per cent is regarded as positive evidence of bone marrow response to some undefined stimulus Positive evidence of this was tound in 87 per cent of the atrophic cases In view of the time consumption in conducting the test it is regarded as of less general application than is the simpler sedimentation test

The \ B Bayliss modification of the Vernes resorcinol test was employed by the authors. The procedure consists in mixing 0.5 cc of a 1.25 per cent aqueous solution, with 0.5 cc of the patient's serum and measuring the degree of turbidity after standing in the icebox over night. This reaction is positive not only in rheumatoid arthritis but also in tuberculosis, syphilis, other infections and malignancy. It appears to the writers that this reaction is probably due to the

presence of serum globulins in amounts higher than normal

The Vernes test was positive in only 58 per cent of the cases of atrophic arthritis and so, while apparently simpler than any other procedure, it is less accurate and is therefore not recommended as a test suitable for widespread routine usage

Four strains of hemolytic streptococci designated as (AB₁₃) (NY₅) and (RB₅) were mixed with dilutions of serum up to 1-320 Tests were regarded as positive which showed agglutination in dilutions over 1-160. In 53 per cent of cases such agglutination was present for at least one strain. For single strains positive reactions were present in 20 per cent for AB₁₃ and 35 per cent for The reactions were negative in most cases of less than six months duration In addition to this, sudden fluctuations in titres were encountered in short intervals during which clinical developments were not correspondingly modified These considerations lead the authors to the view that the agglutination reactions are valuable but exceeded in practicability by two "non-specific" reactions, viz. sedimentation rate and Schilling count

Treatment in General - A recent discussion setting forth an epitome of orthodox therapy in chronic arthritis not hitherto cited and representative of views repeated by many others during 1937 was presented by R. Pemberton¹ in the form of seven recommendations to the general Recommendation number practitioner one is the institution of intelligently conducted rest, usually requiring confinement to bed. This prescription permits the achievement of a state of physiological equilibrium in the major systems of the The warmth afforded by the bed covers helps to open the peripheral blood vessels. The sympathetic nervous system is relieved of the activity required in

the regulation of blood flow in the erect posture. The ptosed visceral organs are relieved of the drag and thus returned to positions more favorable for their The total metabolic normal function turnover is reduced to a minimum and the body mechanisms are then better able to meet the requirements of defense against disease agents whatever they may be in the broad sense. The patients should, however, be instructed to put the involved joints through their given range of motion at least once daily mendation number two is the removal of focal infection after the establishment of optimal "physiology" achieved by bed rest. Emphasis is placed upon gingivitis and the proper analysis of the prostate, which is not so simple as is generally believed. Recommendation number three is the provision of a dietary suitable to the evident requirements of the patient. It is suggested that this requires a more refined approach than that looking toward obesity or emaciation alone. This consideration is given further attention in a subsequent discussion cited later in this article (see page 000). Recommendation number four is the application of the reparative forces available in physical therapy, particularly heat and massage These measures are more potent than any drugs listed in the pharmacopoeta in correcting the functional disturbances of blood and lymphatic flow in the skin and muscles. The use of these measures should be carried out with These procedures should not be applied to the tender joints but directed toward removed sites. Recommendation number five is that caution be used in the administration of drugs for the pain of arthritis Salicylates should be reserved for emergencies Sedatives are valuable aids at the outset of management. Constructive tonic medication

in the form of strychnia, arsenic, and liver extract is favorably considered. Opiates are contraindicated mendation number six is that the use of vaccines be reserved for a small and critically selected group of cases This question is amplified later mendation number seven is the use of measures to prevent and undo angular deformity by maintenance of corrective posture and exercises, whether this angulation affects the chest, the spine as units or the joints themselves Rest in mild opisthotonos may correct kyphosis and alter visceroptosis Breathing exercises tend to expand the narrow thoracic cage Abdominal exercises may contribute to the physiological betterment of function by the support afforded to venous return and the visceral automassage Taken together, these simple measures compensate for some of the secondary consequences of wheel-chair invalidity

Nutrition in Treatment—The nutritional aspects of arthritis have been discussed by R. Pemberton and C. W. Scull 10 It is suggested that while there 15 no complete parallelism of arthritis with any known specific "deficiency disease" many cases of arthritis show graphic evidence of disturbed tissue nutrition, such as bone atrophy, muscle atrophy, anemia, low plasma protein, infiltration with fibrous tissue, degeneration of hyaline substance in cartilage, low basal metabolism low glucose tolerance and reduced variability of skin temperature The evidence of disordered immunity with a high incidence of focal infection may also be reasonably attributed in part to the combined results of nutritional inadequacies

It is recognized that the above changes are often considered "secondary" effects due to some unknown but specific organism, in spite of the fact that there is

no agreement that arthritis is precipitated by any single kind of bacterium

In view of the fact that the chemical substances of the diet constitute the raw material of which tissues are made, it is necessary to entertain the possibility that certain of the functional and organic deviations characterizing arthritis may conceivably arise as end-resultants of deficiencies of those chemical units which make up the structure of fixed tissues

The evident purpose of any therapeutic dietary measure is to achieve in the individual a state of nutrition optimal for the given condition, and meticulous care in meeting these requirements is of first importance in the treatment of chronic disease.

Most arthritics require a diet which provides an adequate supply of calories and is optimally balanced with respect to various components. It should contain at least one gram per kilo body weight of protein of good biological quality It is evident that the conspicuously underweight individual should be given more than a mere maintenance supply of calories, whereas the grossly overweight patient might be given a little less. The emphasis placed upon the quality or source of the protein is based upon the general fact that all proteins are not equivalent in their property of supporting growth or presumably in providing for the regeneration of wasted tissue

.11thritic Diet—The following table itemizes the general requirements for an arthritic diet

The general rôle of nutrition in the arthritic is twofold. First, as regards the antecedent health of tissues as a whole and especially in respect to the extent to which they are open to invasion or disintegration by infection and other factors, and, second, as regards modification, by means of changes in the dietary, of some of the symptoma-

THE GENERAL REQUIREMENTS FOR AN ARTHRITIC DIET

- 1 Calories—To meet the energy requirements of the individual
- 2 Proteins—To meet requirements for growth, maintenance or repair (\bout 1 Gm of protein per kg of body weight, or about 15 per cent of the calories needed)
- 3 Carbohydrates—To supply 33 per cent to 50 per cent of the calories needed
- 4 Fats—To supply 50 per cent to 33 per cent of the calories needed
- 5 Minerals—To meet requirements for growth, maintenance or repair
- 6 Vitamins and other accessory factors— To cover losses and restore depleted reserves
- 7 Water—To cover excretory and temperature control losses
- 8 Bulk-To promote normal intestinal mo-
- 9 Palatability—To meet dietary taste of the individual

tology of the established disease process. Health of tissues depends upon a supply of dietary materials from which resistant tissues can be constructed, and by the same token, necessary repair achieved. This conclusion has obviously preventative implications.

As a practical therapeutic consideration bearing upon the established disease, it may be stated that nearly all arthritics will benefit by the provision of an optimal diet yielding the full caloric requirement and supplying the qualitative demands of the tissues. Such a diet should contain at least 10 gm per kilogram body weight of protein from dairy, meat, or fowl products. From one-third to one-halt of the total remaining calories should be supplied by carbohydrate and the balance made up by fat, compatibly with good digestion. The carbohydrate should be supplied largely in the form of five and ten per cent vegetables Supplementary amounts of vitamins in the form of concentrates are often desirable or necessary to correct

sub-deficiencies cumulative over a long period from inadequate dietaries or from drains upon the supply from infectious factors.

Arthritics with definite infection require a diet higher in total calories than is reflected in the energy output masmuch as infectious processes make demands upon certain unknown compon ents of the ration. This is true of cases showing emaciation. The case presenting clear evidence of gastrointestinal dysfunction and the type of case showing minimal evidence of infectious influence. often receive relief when given rations balanced as above which contain no more calories than are required to meet the basal energy expenditure. A few cases among the latter groups are additionally benefitted by short periods of under feeding. The application of this relatively radical dietary measure is limited to short periods of time and must be conducted with great care

Vaccines—E P Jordan¹¹ presented a critical evaluation of vaccine therapy in rheumatism It is noted that the use of vaccines depends upon the assumption that the arthritis is due to bacterial infection. Those types of arthritis which are not infectious cannot, then, be considered in relation to vaccines. It is further pointed out that vaccines are not used in the treatment of other diseases during the infectious stage, although this is the stage during which their use in arthritis is most often advocated the utility of vaccines depends upon a specific stimulation of immune reactions then it would be necessary to establish the undoubted presence of clearly defined types of organisms in the arthritic lodate there is no one type or organism consistently found in the blood or rissueof arthrities. There remains the possibility that vaccines may afford protection in a non-specific manner and that

groups of protein antigens may, therefore, be effective This is regarded as unlikely, however.

It is further pointed out that desensitization procedures, often regarded as the means by which vaccines are beneficial, depend upon the demonstration of sensitization to definite specific protems. In this respect the demonstration of hypersensitivity is based upon analogy, masmuch as skin sensitivity, the chief objective method now available for direct evaluation of the state of hypersensitivity remains difficult of interpretation in arthritis It is evident that much more needs to be understood underlying mechanisms of immunology before a satisfactory basis can be made for evaluating divergent claims for the superiority of various procedures and techniques used in the preparation of and administration of the diversely constituted mixtures, collectively called vac-These considerations are applicable whether the preparations are suspensions of bacterial organisms, attenuated or dead, filtrates, whether these are obtained from stock cultures or from autogenous sources, foci, excretions or body fluids

In addition to the general theoretical difficulties reflected by Jordan, it is further emphasized that the interpretation of results in clinical groups is not casy. It is pointed out that classical theumatic tever is a self-limited disease with respect to its active phase and is not susceptible to close analysis with respect to vaccine therapy. Jordan recognizes a somewhat more chronic condition called, for lack of a better name. rheumatic infection, which presents an abnormally slow sedimentation rate in contrast to rapid rate of classical rheumatic fever Such patients present features of hypersensitivity in the true allergic sense, in that they present marked exacerbation of symptoms following minor infections Among this group it appears logical and practical to use specific desensitization through the use of bacterial organisms or their products.

In atrophic arthritis the utility of vaccines is regarded as undemonstrated. There appears less support for the employment of vaccines in hypertrophic arthritis. The use of vaccines in the specific arthritides is less widely used, and other more effective measures are usually applied to gonococcal and pneumococcal infection. The routine use of vaccines is deprecated and their administration in selected cases under controlled conditions only is advised.

Bile Salts - Jaundice - The influence of jaundice upon the course of chronic atrophic (infectious) arthritis, has been further studied by P Hench,12 with the aim of providing a therapeutic use of the phenomenon of remission or arrest induced during the course of the arthritis and primary fibrositis by a spontaneously occurring laundice. The mechanism by which the remission is produced is not yet clear However, the fact that there is a causal relationship appears from the fact that 100 per cent of nine cases of fibrositis experienced complete relief, while 63 per cent of 19 cases of atrophic arthritis were completely relieved, while the remainder experienced partial relief. The effect of the jaundice appears to be related to the extent rather than to the kind of jaundice, and the zone of therapeutic efficacy is characterized by a level of eight to ten mg of bilirubin per 100 ml of serum The remissions lasted from three weeks to 45 months, with an average of three times to the duration of the jaundice Relapses occurred in 48 per cent of the cases and partial return of symptoms appeared in 39 per cent of

It thus seems that some metabolic influence operative during the course of clinical jaundice exerts in a significant number of instances a temporary beneficial influence on the course Attempts to reproduce of arthritis some of the known conditions extant during jaundice have been unsuccessful in providing relief in the experience of Hench, although H E. Thompson and B L. Wyatt¹³ report that the combined administration of bilirubin and bile salt (sodium dehydrocholate) in nine cases led to remissions of atrophic arthritis The dosage employed was 10 mg bilirubin and 40 mg bile salt per kg body weight administered intravenously Such a combination is the only one of the several combinations reported to date which has approximated the influence of the spontaneous jaundice Either component used alone is without effect, according to Hench, Thompson and Wyatt, N Sidel and W B Rawls In the experience of Hench, bile salts, decholin, ox bile and human bile by stomach tube and by proctoclysis are without effect Transfusions of highly jaundiced blood is also meffective. Even an experimentally tested therapeutic jaundice produced by administration of toluvlene diamine proved unavailing. Pursuing the view that the influence may arise from the autolytic products arising in the liver during jaundice, H. M. Margolis administered a beef liver autolysate intravenously Rather than favorably influencing the arthritis an exacerbation of symptoms was produced

Gold Salts—The rather widely held view that some chemotherapeutic measure may sometime be found to arrest those cases retractory to the procedures now available, lends interest to the critical evaluation of gold salt therapy in chronic arthritis presented by R. G. Snyder, F. J. Lust, C. H. Traeger and LeM.

C Kelly.14 A wide variety of organic and inorganic compounds of gold are employed, including allochrysin, soganol, myoral, sanochrysin, myochrisin, lipaural, chrysalbin, lopion, aurocein and gold sodium thiosulfate. These substances have apparently been more widely used in Europe than in America Wide ranges of dosages are used at the hands of various practitioners. It is the view of the authors that all gold salts are toxic and their employment should be carried out with caution. It is pointed out that gold is largely excreted by the way of the kidneys and that a portion is deposited in the mesenchymal tissues. In common with other agents small amounts may produce a stimulation of cellular activities while larger doses are toxic Because of the cumulative effect, injections are usually given at weekly intervals for periods of from eight to ten weeks, followed by rest periods of one to two months

In order to evaluate gold therapy 100 selected cases were studied Only patients who had been resistant to other forms of therapy were included in the series. No subjects were included who presented a history of skin, liver, kidney or intestinal irritability, or blood dyscrasia Intravenous administration of gold sodium thiosulfate in doses of 5 to 10 mg up to the point of tolerance was carried out. All subjects were closely followed with respect to blood count, sedimentation rate, urine analysis and symptoms of skin irritation. In 11 patients mild dermatologic eruptions appeared. One patient experienced a severe cutaneous reaction and one subject developed dyspnea due to edema of the glottis Both of the latter recovered completely from the arthritis as compensation for their unpleasant experiences. On the whole, no spectacular results were encountered although 45 per

cent of the cases presented varying degrees of clinical improvement. It is worthy of note that about 35 per cent of the hypertrophic cases were apparently improved by these measures. This is in contrast to the experience of Forestier. This difference may be attributed to the selection of cases.

To the authors it appears that hypertrophic arthritis is due to more than degenerative influences and includes in addition low grade infectious or toxic factors. This latter view is often minimized regarding etiology but to the Reviewers it harmonizes with the facts seen in the clinic The authors conclude that gold salts should be used only in selected cases, which can be carefully followed The risks incurred in the use of gold salts should be recognized as significant P S Hench15 cites a mortality rate of three per cent in one series of cases. The possibility of reward should be regarded as uncertain until further controlled study reveals the kinds ot cases most likely to benefit and the kind of gold compounds most efficient and least toxic

Physical Therapy - The value of the application of physical therapy to the treatment of arthritis has been emphasized by 1º H Krusen 10 Except for a few methods which require claborate equipment and control, the procedures of physical medicine which are of the most value in the treatment of arthritis can be conducted under intelligent supervision in the home of the patient. It is pointed out that while physical rest is of prime importance in the therapeutic regimen, complete physical mactivity is as hazardous as overactivity A balance of activity within the range of functional capacity is the end as well as the means by which recovery is to be attained. The use of heat is employed as a means of modifying some of the physiological deviations toward normal Relaxation of tense muscles, improvement of peripheral blood flow and heightened cutaneous secretion may be achieved by the application of heat The wide variety of measures by which heat may be applied is elsewhere described in the Cyclopedia In addition to the usual measures of hot air and water. passing mention may be made of the use of molten paraffin, which provides a convenient and inexpensive way to subject tissues to elevated temperatures The use of exposure to cold as a general metabolic whip, and as a peripheral vascular exerciser when applied alternately with heat is regarded as valuable Exposure to sunlight is considered as an effective agent in a program of "tonic" medication Massage directed at tissues removed from the involved joints aids the mechanics of the partially embarassed circulation and thereby corrects the consequences associated with vascular and lymphatic stasis Manipulation of joints partially fixed, in which the active process is quiescent, may be helpful if employed with conservatism and at the hands of an orthopedist

The prevention, as well as the correction, of deformity is one of the important factors in the care of the arthritic. While the application of many of these procedures requires the talent of the specialist, there are several general measures that can be advised and some common errors in practice that can be avoided The use of splints or plaster shells helps provide relaxation and so prevent contraction Avoidance of the use of pillows under the head and knees is recommended masmuch as such practices tend to induce deformity return toward normal requires the use of graded exercises including not only the involved joints but of the body as a whole Attention should be directed

then toward achievement of optimal body mechanics. This may be attained by the application of corrective exercises and the development of proper postural habits. Underwater exercises are recommended as being well adapted to the movement of joints with a minimal amount of strain Occupational therapy adapted to the capacity of the patient not only permits physical exercise but also provides a psychological stimulus which is of great value to the partially incapacitated chronic patient

In addition to the influences exerted by heat and cold as mentioned above, Hydrotherapy may also modify physiological function through the mechanical factor of pressure The use of physical measures in the management of intestinal dysfunction is regarded as important despite the fact that their application is limited Such measures consist of massage over the area of the colon coupled with lavage. It is likely that the influence of large quantities of fluid within the colon extends beyond the range of the mechanical factors although these are as vet not clearly defined Routine and uncritical application of this measure is deprecated. The application of low frequency currents in the involuntary stimulation of muscular activity is regarded as being of limited value

Emphasis is placed by Krusen on the utility of *massage* in the treatment of *fibrositis*. The nodules of inflammatory or indurated connective tissues often may be made to disappear by deep pressure. Caution must be used in view of the fact that liberation of the material from these nodules may give rise to systemic reactions similar to those produced by overdosage with vaccines. The application of *fever therapy* appears to hold little promise of value for the chronic arthritic although as noted elsewhere, is of importance in the treat-

ment of gonococcic arthritis. Diathermy and inontophoresis with acetylcholine and histamine may have value when used in conjunction with other measures, but their influence can be utilized chiefly as a part of institutional care

GONOCOCCIC ARTHRITIS

Diagnosis-The diagnosis of gonococcic arthritis has been discussed by C S Keefer and W. W Spink 4 Upon the basis of 140 cases studied extensively and critically, the criteria regarded as essential include a history of a recent attack of gonorrhea, evidence of gonococcic infection in the genital tract, a positive gonococcus complement fixation reaction of the blood or synovial fluid. and the presence of gonococci in the synovial fluid The clinical features associated with gonacoccic arthritis are helpful in diagnosis The onset is abrupt. inflammation of the periarticular tissues and synovial membrane is intense. The involvement is often polvarticular. Tenosynoritis is regarded as a significantly common feature. The disease may in some instances be apparently precipitated by respiratory infection, surgical operation and pregnancy Gonococci may be recovered from joint fluids despite negative cultures from the genito-urmary tract and without a history of infection There is usually fever, leukocytosis, and an increased sedimentation rate. Exacerbations of the arthritis may be induced by prostatic massage or reinfection

.lcute polyarthritis occurring with conjunctivitis or iridocyclitis and a cutaneous cruption resembling psoriasis is suggestive of gonococcie arthritis

Examination of the synovial fluid may aid in the diagnosis. Anacrobic culture of fluids from gonococcal arthritis is positive in 26 per cent of cases. The gonococcus complement fixation is posi-

tive in the fluids of 66 per cent of cases. This is higher in patients with sterile fluids than in patients with infected synovial fluids. Positive complement fixations were not encountered in the synovial fluids when the positive reactions were not obtained in the blood serum. The total cell count is higher in infected than in non-infected fluids while the sugar content is lower in the former than in the latter. Positive blood cultures are rarely found. The bacteriolytic capacity of the blood increases during the course of the disease and 85 per cent of the cases showed positive reactions.

Treatment of Gonococcic Arthritis -The treatment of gonococcic arthritis is approached from three angles Specific serum therapy does not appear to be very successful although it is effective in clearing the blood of organisms and its application should be limited to cases of bacterenna Fever therapy utilizing the thermolability of the organisms is widely accepted as an effective measure in acute Its influence is much less in the chrome phases of the disease. There is a revival of the use of chemotherapic measures with the introduction of sul-A few cases treated with fanilamide sulfamilamide have responded more promptly than by any other measure, with a disappearance of organisms from local lesions and a remission of the articular symptoms. It may be noted that limited experience with the use of sulfanilamide in chronic atrophic arthritis at the hands of several workers shows little, if any, promise of value

Aspiration of joints with effusion is advised. Where the fluid is thick and contains excessive quantities of fibrin the joints are opened and irrigated through incision into the capsule. After washing, the joint is closed and placed in traction and motion started as soon as possible without pain.

General treatment of the chronic cases which present features common to various infections such as loss of weight, anemia, and muscular atrophy, is conducted along the usual reconstructive lines

SPONDYLITIS ADOLESCENS

Differential Sedimentation Tests -A "serological" procedure recently extensively studied and applicable to the diagnosis of rheumatic diseases is presented by H Coke.5 The test is based upon the colloidal properties of the serum and the ability of vanadium salts to precipitate some of the colloidal substances The procedure is designated as a differential sedimentation test, so called because treatment of the serum with heat and with ether modifies the amounts of precipitate produced by a given series of vanadium solutions at different hydrogen ion concentrations. While the technic is based upon physical chemical principles the evaluation of results is based upon empirical and arbitrary definitions This expedient apof concentrations pears to be justifiable and clinical inter-

The differential sedimentation test is performed as follows Blood, withdrawn from the antecubital vein of the fasting patient, is placed in a sterile test tube The blood is allowed to clot and stand tor 16 to 24 hours. This period of standing is required to permit the establishment of equilibrium between the components of the cells and the serum. The serum is separated from the clot and centrifugated to remove the cells. One and two-tenths ml of the clear serum is diluted with an equivalent quantity of distilled water Two-tenths of an ml aliquot portions are then transferred to five test To each of these is successively added an equal portion of colloidal acid vanadate reagents from a series empiri-

pretations are not thereby handicapped

cally designated by numbers 25 to 29. After standing from 6 to 12 hours the amounts of precipitate in each tube is estimated. Such determinations may be made by estimating the nitrogen or vanadate or preferably by refractometric measurements, of alkaline solutions of the precipitate. The amount of precipitate formed by 15 mg of protein is regarded as a reference point and this is empirically designated as 40 units. The mixture with which this quantity is formed is plotted as abscessas, against refractometer or interferometer units as ordinates Such a plotting of data for normal sera gives a curve which is nearly perpendicular and intercepts the 40 unit reference line at five. In pathological sera the curve usually tends to be less nearly perpendicular and to intercept the base line at positions from 15, in cases of hypertrophic (chronic, toxic, osteo) arthritis, to 36 in cases of atrophic (rheumatoid) arthritis, and atrophic spondylitis (spondylitis adolescens)

The influence of heating on the colloidal stability of the blood serum is measured by subejcting diluted serum cone volume of serum to one volume of water) to a temperature of 1308 (56) C) for 30 minutes. The precipitation curve is estimated as outlined above for the unheated serum. The quantities of precipitate produced are less than obtained with the untreated specimen. This difference is associated with a decreased aggregation of particles and an increase in viscosity. The former phenomenon is evident on dark field examination and the latter by viscosimetric measurements. In normal sera the difference between the heated and unheated curves is constant The magnitude of the heating effect is increased during the period of generalized bone demineralization of rheumatoid arthritis and decreased during the stage of mineralization of the spinal ligaments in syondylitis. In general the heating effect, or "green field," is increased by infection and decreased by long standing infective foci, by the presence of viable organisms in the serum, and by allergic It may also be increased by toxemia, the introduction of antigenic substances, by x-radiation and exposure to ultra violet light. Although a variety of factors may be involved, some of which are undefined, the authors regard an increase as related to an elevation in the level of serum globulin. Thus, in the view of the authors the green field is an index of the patient's response to a stimulus and hence is a measure of the patient's resistance. Whether this interpretation be correct cannot be determined in the opinion of the reviewers on the basis of available data. This does not detract, however, from the use of this concept as an hypothesis worthy of more extensive trial.

The stability of the serum is further studied after treatment with ether. One inl of the serum is shaken with an excess of diethyl ether for one minute. after which the mixture is allowed to stand for 12 hours. The extracted serum is pipetted out from the ether laver and transferred to another tule ether remaining is evaporated off by incubation at 986 F (37 C) for 45 Precipitation of aliquot portions of the serum treated with vanadium reagents is carried out and plotted as in the procedures outlined above ether treatment there is a le-sened stability with a resultant increased precipitability of the proteins especially of the globulms. The increase as compared with the untreated specimen is designated as the red field effect. The red field is rarely decreased below the normal. According to the authors an increase in the red field represents an overpowering of the detoxifying mechanisms or a resultant of

the long continued stresses of chronic invalidity. It is interesting to note in the light of the influence of jaundice on arthritis cited in this article that this clinical condition is associated with a decreased ether effect Chronic hypertrophic arthritis (toxic ostcoarthritis) and the latter stages of atrophic spondylitis (spondylitis adolescens) are characterized by increased red fields

A significant contribution on the early diagnosis of stondylitis and a therapeutic measure worthy of more extensive trial is made by S G Scott 6 The syndrome described by Scott corresponds to atrophic spondylitis with calcification of the anterior common ligament. The author regards the latter as well as the terms Strumpel-Marie disease, theumatoid spondylitis, poker-back spine, spondylose thizomelique as madequate descriptions of the condition. He prefers the term spondylitis adolescens as more adequately descriptive of the clinical picture Bilateral sacrollutiv is the pathognomonic teature which characterizes the condition This appears from 12 to 26 years. The evidence of this situation may not be apparent to the subject in the form of localized pain in this region, but is always evident in rochtgenograms the early stages, inflammation may be evident in the sacroiliac joint and the latter stage is marked by ossification The recurrent development of rheumatoid symptoms in patients under 25 years of age should lead to their being regarded as possible subjects of this disorder, and not blandly dismissed as due only to growing pains or tibrositis These cases are marked by severe pain in the knees, wrists, arms, thorax, shoulders, pelvic girdle, hips, ankles, calves, and thighs Using these clinical guides and the roentgenographic evidences of bilateral sacroilutis, Scott believes that early diagnosis is possible, thus anticipating the ossification and fusion of shoulder and hip girdles which marks the final distressing picture of the fully developed disease

As a useful adjunct to the usual medical measures Scott recommends the administration of wide field roentgenradiation. Exposure to mild systemic radiation is of principal value in the early active stage of the disease Doses of 80 to 100 r are given of 130 to 140 KV, using an aluminum filter Areas of 12 to 14 inches (30 5 to 35 5 cm) in diameter are irradiated Treatments are given two times per week in series of 12 doses The mechanism by which this agency exerts a beneficial influence is not fully known, but the favorable responses produced in a number of cases would appear to justify its conservative application to additional patients

RHEUMATISM IN CHILDREN

Diagnosis and Treatment—F J Poynton and B E Schlesinger⁷ have presented a summary of data including material bearing upon the diagnosis and treatment of acute arthritis in children and chronic arthritis in the adult Some aspects of the former problem may be cited particularly as this summary defines features often overlooked

To the Reviewers there emerges from the data a picture of the child with rheumatic fever, apparently made so by inherited deficiencies, unfavorable environmental factors, subject to infection, but probably not a carrier of disease Many of his tissues are the site of pathological The lesions in his heart involvement are significant and require attention, but equally important manifestations appear in his lungs, liver, and gastrointestinal tract Hepatic disturbances may be responsible for his toxic symptoms during acute phases, constituting as great a risk as cardiac failure in the critical stage

The organic disturbances are associated with the well known sequence of widespread tissue changes involving (1) a swelling of collagen fibers of connective tissue, with small zones of necrosis; (2) a mobilization of mesodermal connective tissue and wandering cells; (3) scar tissue formation. These processes underlie the production of the Aschoff bodies which are regarded as pathognomonic for the rheumatic condition. The distribution of these special lesions is partly determined by traumatic factors and appear at sites subjected to mechanical friction There is in addition widespread damage to the capillaries

The precise nature of the agents responsible for the rheumatic illness of the arthritic child is still a matter of debate among his medical advisers. His blood and tissues do not uniformly yield viable micro-organisms, and when positive cultures are obtained the same strains do not always appear, his blood serum does often show high concentration of antibodies against streptococci, but this evidence is not sufficiently specific to implicate any single strain. This observation may be amplified by recalling the report of Dawson that in rheumatic fever agglutinins for hemolytic streptococci are within normal levels whereas the antistreptolysin titres are increased situation may be contrasted with that in atrophic arthritis wherein the agglutinins are increased and the antistreptolysins are normal. Furthermore, relapses may occur when the level of circulating antibodies is at its height. It appears to the authors that the most probable explana tion of the patient's condition arises from the influence of streptococcal infection which lowers the defense against a virus This view is based upon (1) the finding of virus bodies in pericardial fluids, and by (2) the similarity of lesions to those produced in known virus diseases While

the patient presents similarities in his remissions and relapses to those of his contemporary sufferers from tuberculous infection, the writers regard this as parallelism rather than an identity as is claimed by some. The possibility that exaggerated sensitivity or allergic phenomena are responsible for the symptoms of the rheumatic is held to be plausible but perhaps unnecessarily complicated.

The therapeutic management of the rheumatic child is first medical and then The medical adviser becomes social should recognize that the problem is not cardiac alone The value of directing attention to the general condition, pulse rate, temperature, physical signs, sedimentation rate, appearance of chorea-like symptoms is shown Protection from factors favorable to development of in fection, especially in tonsils, is shown to be important. The most frequently encountered electrocardiographic features are illustrated. Plans of organization for special homes with trained nursing care and sympathetic medical supervision is Graded exercise, "tonic" medication, educational adjustment. are significant parts of the rehabilitation of the rheumatic child. In addition to the drugs usually employed the use of nirvanol is suggested. This drug is alpha-phenyl-ethyllydantom, a product of the combination of urea and glycol is administered in daily oral doses of 0.2 to 0.25 grams per day for children up to nine years of age and in doses of 03 grams up to 14 years of age. The drug may induce cutaneous rashes but the arrest of choreic manifestations which usually follows is regarded as adequate compensation for the risk. The precipitation of acute permanditis is a sections but not frequent complication of the use of the drug

As an index of the *prognasis* for the rheumatic child, the results of manage-

ment of 1,000 patients may be cited Of this group, 76 died, 40 were discharged as cured, 200 were not available for subsequent re-examination, 680 regularly followed appeared to be in good health These figures show that while the disease is a serious one, its etiology not fully known, it is not nearly the hopeless one it is often regarded to be

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CARDIOVASCULAR SYSTEM

By Albert W Bromer, AB, MD

I. INTRODUCTION

Among the outstanding contributions on cardiovascular disease during the last few years have been studies relating to experimental cholesterol arteriosclerosis, periarteritis nodosa, factors responsible for auricular fibrillation without evidence of organic heart disease, incidence of coronary artery disease in individuals under 40 years of age, interpretation of precordial leads of the electrocardiogram, dissecting aneurism of the aorta, sympathectomy in essential hypertension, the mechanism of left and of right ventricular failure, total thyroidectomy in the treatment of nonthyrogenous congestive heart failure and of angina pectoris, pericardiectomy in chronic adhesive pericarditis, lymphedema of the extremities, and the benefit of passive vascular exercise in obliterative peripheral vascular disease

By feeding cholesterol, T Leary reproduced in rabbits lesions similar to those of human atherosclerosis In evperimental atherosclerosis, the first manifestation of vascular lipoidosis is the appearance of lipoid in spaces beneath the endothelium of the vessels. As the process ages, it is common to find deeper invasion by some of the lipoid cells as fibrosis of the inner layers takes place When lipoid cells accumulate, even in isolated groups, necrosis of the cells tends to occur, with freeing of cholesterol in crystal form (atheromatous "abscess")

Study of the histologic changes present in fatal cases of human coronary sclerosis revealed that the dominant change in the coronary arteries of individuals 25 to 55 years of age consists of fibrosis leading to narrowing of the lumen, and that the outstanding cause of death is

thrombosis following subendothelial necrosis. In individuals from 47 years to extreme old age, the dominant lesion consists of collections of lipoid cells with a tendency to atheromatous necrosis, giving rise to atheromatous "abscesses", in this group rupture of an atheromatous cavity in the lumen, with secondary thrombus formation, is the usual cause of death

The conclusion is drawn that atherosclerosis is a disease of noninflammatory origin, and is not the inevitable consequence of age-as it appears in the voung and may be highly selective in its localization The process is primary in the intima-stress favoring the localization The increase of atheroof the lesions sclerosis observed in diabetes after use of diets excessively rich in fats supports the experimental findings in rabbits following feeding of cholesterol The inheritance of a poor cholesterol metabolism appears to be associated with the tendency to an early death from coronary sclerosis. As far as is known, no cholesterol is synthesized in the human body all of the supply is ingested. Man is the only animal that ingests eggs and milk throughout lifetime, and, as far as is known is the only animal which dies in early life from coronary sclerosis and which acquires atherosclerosis almost universally in advanced life

Penartentis nodosa is an uncommon condition but its incidence probably greatly exceeds its recognition clinically and pathologically. The etiology is unknown, but it appears to be closely associated with the "rheumatic group" of diseases. As pointed out by W. S. Middleton and J. C. McCarter, the most common symptoms are fever, chlorotic marasmus, polyneuritis and polymyositis, striking abdominal manifestations (cramps, vointing, diarrhea, melena and perforation) and nephritis. Anemia with

leukocytosis and eosinophilia may be present Hypertension is frequently encountered. Whenever the question of periarteritis nodosa arises, biopsy of accessible nodules or of involuntary muscle should be performed. Treatment is entirely empiric.

As pointed out by R D Friedlander and S. A. Levine, the mode of onset of attacks of auricular fibrillation, particularly the paroxysmal type, with absence of other signs of heart disease, may be the result of a "trigger" mechanismpossibly related to the adrenal gland-in individuals with hyperreactive or unstable nervous systems. In experiments on typerthyroid animals transient auricular fibrillation can be produced by doses of epinephrine too small to alter the cardiac rhythm of normal animals or those with hypothyroidism. Many of the patients studied by the authors resembled in physical appearance and behavior patients with active hyperthyroidism

According to L H Nahum and H E Hoff auricular fibrillation is produced by the interaction of two factors on the auricular invocardium, viz. (a) preponderant vagus activity, and (b) an E factor, such as thyroxine, electric shock or possibly simple auricular distention Through the injection of acetyl-B-methylcholine chloride (which produces the same effects on the pacemaker as stimulation of the vagus nerves), the normal mechanism of four hyperthyroid patients and four electrically stimulated cats was converted into auricular fibrillation hyperthyroidism, overactivity of the vagumay develop reflexly from the tachycardia and the growing hypertension so often present, in addition increased sensitivity to the vagus substance is believed to exist naturally in such patients mitral stenosis, distention of the auricle may contribute the necessary stimulus

In a study of Lead IV of the electrocardiogram of 50 normal children (ranging in age from 1 month to 16 years) by H Rosenblum and J. J Sampson, 64 per cent of the tracings showed an upright T4, 32 per cent exhibited a diphasic or an isoelectric T4, and in only four per cent was T4 inverted The right arm electrode was placed over the left second, third and fourth sternocostal junctions, and the left arm electrode over the sixth to eighth thoracic spines on the posterior Also M Rabinow, L N chest wall Katz and A Bohning found diphasic (with the first phase upright), polyphasic, or upright T-waves in Lead IV to be common in normal children, especially in the younger groups. Children with active rheumatic heart disease showed a higher percentage of upright T-waves in Lead IV than did normal children of the same age. In normal children, the contour of Lead IV was tound to alter considerably in tracings taken a few months apart. Upright Γ_4 -waves tended to be more frequent in children with thin chest walls and narrow thoracic cages

In electrocardiograms of 200 normal men and women ranging in age from 20 to 35 years, R. A. Shipley and W. R. Hallaran found the T-wave in Lead IV invariably inverted. In a study of 26 adults with an upright or diphasic T-wave in Lead IV as the only definite electrocardiographic abnormality, reported by J. Edeiken, C. C. Wolferth and F. C. Wood, 17 had a clinical diagnosis of angina pectoris, two, questionable angina pectoris, four, old coronary occlusion, one, congenital heart disease. Only one of 299 college students studied by the latter clinicians had an upright T4 with normal limb leads, and he was found to have rheumatic aortic insufficiency. In 81 children (48 with rheumatic heart disease and 33 with no evidence of heart disease), upright T₄-waves were found in approximately 25 per cent of each group A T₄-wave isoelectric, or diphasic, with an upright component of 1 mm or less, has been found in individuals with abnormal limb lead electrocardiograms in whom the presence of definite heart disease could not be proved; but, in the absence of digitalis medication, an upright T₄ has not been seen in any normal adult, with the anterior electrode placed at the apex

In an electrocardiographic study by H D Levine and S A. Levine of 44 patients (subsequently examined postmortem), myocardial infarction was present in 12 of 15 cases in which Q4 was absent, two cases with bundle branch block and one with tuberculous pericarditis also showed an absence of Q4, but no myocardial infarction Of 15 cases with a small Q_4 (2 mm or less) about one-half had myocardial infarction. In 11 cases in which the heart was normal and in one with posterior infarction Lead IV was normal In 16 of 100 consecutive ambulatory cases of angina pectoris, Q4 was absent, and in 11 of 16 customary limb leads were essentially normal

The cure of chronic constrictive pericarditis by operation is one of the most satisfactory advances in the surgery of the heart. In an analysis of 15 cases of chronic constrictive pericarditis, presented in the St Cyres Lecture of the National Hospital for Diseases of the Heart in London, P D White cites the following clues in diagnosis (1) Insidious onset of dropsy in a young person, (2) preponderant liver enlargement and ascites, (3) increased prominence of the jugular veins, (4) normal or relatively normal heart in the presence of dropsy without nephritis, (5) low blood and pulse pressure and paradoxical pulse, (6) x-ray evidence (poor pulsation, calcification, chronic pleuritis), (7) electrocardiographic abnormalities (low voltage or coronary T-waves in chronic disease in early youth), and (8) a previous history of acute pericarditis or polyserositis In differential diagnosis, consideration must be given to the possibility of (1) mitral stenosis, (2) polyserositis (including instances of perihepatitis, or frosted or iced liver—zuckergussleber), (3) primary cirrhosis of the liver, (4) nutritional edema, (5) tricuspid stenosis, and (6) mediastinal tumors Of 12 cases on whom the Delorme operation cases on whom the Delorme operation was performed by the same surgeon, there has been complete cure in six, and one other has been relieved to a marked degree

Lymphedema of the extremities has a multiple etiology Studies of the anatomy and physiology of lymph vessels, such as that by C K Drinker and M. E. Field have aided immensely in understanding the condition Lymph stasis occurs primarily as a result of obstruction produced by inflammatory or noninflammatory processes, or by lymphangiecstatsis, which occurs in association with congenital lymphedema When obstruction occurs, intralymphatic pressure increases, causing dilatation of lymph vessels with subsequent insufficiency of the valves, torcing the lymph to seek new channels which are supplied madequately with valves, the protein content of the lymph increases and fibroblasts proliferate. As a result of the increased quantity of lymph in the tissues, attacks of acute inflammation may occur, producing thrombosis of lymph vessels, more stasis of lymph and, hence, more fibrosis There is a vicious cycle, consisting of stasis of lymph, fibrosis, inflammation with further stasis, and, as a result, more fibrosis

E V Allen and R K Gormlev have divided cases of lymphedeina of the ex-

tremities into two main groups, viz, (1) noninflammatory and (2) inflammatory The noninflammatory group is subdivided into (1) primary, which includes (a) lymphedema precox, which affects female predominantly, with onset during adolescence, and (b) congenital, which includes the familial type, known as Milroy's disease (1892); and (2) secondary, which may result from occlusion of lymph vessels by metastasis of malignant tissue, pressure outside of the lymphatic trunks as might occur in lymphsarcoma or Hodgkin's disease, surgical removal of lymph nodes or treatment with radium or x-ray. The inflammatory group may be subdivided into (1) primary, and (2) secondary—resulting from lymphangitis secondary to known causes, such as venous stasis, trichophytosis, systemic diseases, local tissue injury or inflammation, and filariasis

Lymphedema must be differentiated from (1) the edema of general systemic diseases, such as myocardial failure, nephritis and myxedema, (2) deep thrombophlebitis, (3) lipodystrophy, (4) enlargement of limb due to arteriovenous fistula, and (5) sarcomas, lipomas and neoplasms of bone

Medical treatment is of little or no value unless instituted early, when the edema first appears, 1 e, before the limb is greatly hypertrophied with connective tissue Elevation of the extremity and application of a rubber roller bandage may then prove of benefit. Attacks of acute lymphangitis ordinarily sub-ide spontaneously, but recovery is hastened by elevation of the limb and application of hot moist packs. Selection of cases for surgical treatment is governed by the etiology and severity of the lesion. For example, in the presence of malignancy, Hodgkin's disease or pelvic tumors, there is no need for operation Operation is predominantly a plastic procedure, con-

sisting of the removal of large valveless lymph spaces and hypertrophied connective tissue.

Passive vascular exercise, obtained through rhythmic alternation of the environmental pressures (Pavaex therapy), has been employed quite extensively in the treatment of obliterative arterial diseases of the extremities According to L G Herrmann, the greatest increase in the arterial circulation is brought about by from two to four cycles of alternating pressure, each cycle consisting of a gradual rise to 20 mm of mercury positive pressure and a fall to 80 mm of negative pressure—the pressure being predominantly in the phase below the existing atmospheric pressure Approxmately 100 hours of passive vascular exercise, given at the rate of at least five hours each day, is sufficient to stimulate the development of an adequate collateral circulation in most patients with obliteration of the major or secondary arteries of an extremity when the arteriolar network is relatively normal Repeated calorimetric and oscillometric studies have shown that the collateral circulation thus obtained remains active and in many instances becomes more active for many months after the treatments have been discontinued

The use of *local hyperthermia*, produced by preheated dry an averaging 104 F (40 C), in conjunction with passive vascular exercises tends to overcome peripheral vasospasm. Arteriovalerous obliterans with or without gangrene and with or without the association of diabetes has proved to be amenable to passive vascular exercises, since the ischemia can be quickly overcome and the gangrene made to demarcate Passive vascular exercise, however, is primarily a means of preventing serious complications and not a cure for extensive gangrene. It offers only temporary

relief from the circulatory disturbances in true thromboangutis obliterans (in which there is usually an extensive obliteration of the arteriolar and small arterial beds). The effect of passive vascular exercises is enhanced by local hyperthermia in intermittent claudication. Acute or subacute thrombophlebitis is a definite contraindication to the exercises. Varicose veins are not affected by the procedure. Good results are obtained in the less malignant forms of cellulitis of the foot associated with trophic lesions.

II. TREATMENT OF PERIPHERAL VASCULAR DISEASE

Alternating Suction and Pressure—Since the introduction of alternating suction and pressure as a method of treatment of peripheral vascular disease (described in 1933 almost simultaneously by two groups of investigators, vis, E M Landis and J H Gibbon, Ir, and M R Reid and L G Herrmann), the value and limitation of its use have been fairly well established Almost all reports accord it a certain place in the armamentarium of treatment, but, as stated by N W Barker,1 it has not proved superior to certain other simpler methods of therapy Ordinarily good results follow its application when improvement can be expected from other measures, and when benefit does not follow other measures passive vascular exercise usually proves useless. In the evaluation of this type of therapy it must be borne in mind that occlusive arterial diseases, particularly thromboangutis obliterans, are subject to exacerbations and remissions—being influenced by factors such as climate, season and barometric pressure, and also that rest in bed is the most important phase of all successful therapeutic procedures

According to E V. Allen and G. E Brown,² the best results with alternating suction and pressure at the Mayo Clinic have been obtained in ischemic neuritis, in acute arterial occlusion and in frost bite of moderate degree. Healing of ulcers may be induced. The contraindications to treatment with alternating suction and pressure are associated venous occlusion of any type and the presence of local infection and cellulitis.

All investigators agree that alternating suction and pressure are of particular benefit in arteriosclerosis obliterans With the apparatus of Herrmann, J H Conway³ observed improvement in 80.5 per cent of 36 cases of arteriosclerosis obliterans affecting the major or secondary arteries of the extremity The development of "collateral circulation" does not signify the production of new arteries but causing arteries already present to function at a higher physiologic level If the capacity for distention of the arterioles and capillaries does not exist, but little help can be expected from this method of therapy. In cases of thromboanautis obliterans with gangrene the treatment has been disappointing. Among the reasons for the differences in results obtained in the treatment of thromboangutis obliterans and obliteration due to arteriosclerosis may be the fact that in thrombo-angutis obliterans the veins as well as the arteries are involved. Alternating suction and pressure may prove of particular value in the treatment of older patients with occlusive vascular lesions due to arteriosclerosis, in that repeated intravenous injections of typhoid vaccine are not tolerated well by such individuals, and sympathectomy with the increased risk due to advanced age is not an advisable procedure

In regard to its use in cases of sudden arterial occlusion, W Bierman⁴ states that in view of the spontaneous improve-

ment which occurs occasionally and the possibility of surgical removal of the embolus if the patient is seen sufficiently early, the exact value of alternating suction and pressure is still to be decided. Such cases always must be regarded as a true surgical emergency and should be admitted to the hospital during the first few hours after the acute occlusion in an effort to save the limb

In many cases of organic peripheral arterial disease arteriospasm adds to the obstruction caused by the organic lesion Such spasm is prominent in the acute obstructions, especially embolism and thrombosis Arteriosclerosis is almost free of arteriospasm except when thrombosis occurs, while, on the other hand, thrombo-angutis obliterans is frequently complicated with considerable arteriospasm. Vasospasm may be relieved by the (1) increase of environmental teniperature as by (a) the heating of the diseased limb itself, (b) the warming of the body by blankets and heaters, or (c) the heating of one or two limbs not being treated, (2) fever therapy, (3) anesthesia (local, spinal or paravertebral), and (4) vasodilating drugs (alcohol, theobromine and mecholin) order to reduce reflexly the vasoconstrictor tone in the lower extremity, E M Landis and L H Hitzrot? applied an electric pad around one arm while administering 80 to 120 mm of negative pressure for 25 seconds and positive pressure of from 60 to 80 mm of mercury for five seconds, and M. R. Reid and I G Herrmann used preheated air at 102 to 105 F (389 to 406 () to heat the treated limb and in addition prescribed whisky, while applying 80 mm of negative pressure and 20 mm of mercury positive pressure-alternating in cycles from two to four a minute

A Edwards⁶ describes a device consisting of two 75-watt tubular warmers bolted on the interior of the suction pressure treatment chamber. Warmth locally applied in this manner is capable of maximum vasodilatation and increases the effectiveness of the suction. Moreover, the local increase in metabolism caused by the raised temperature assists in the process of healing. The temperature selected for each patient is that which proves most comfortable, never being above 110° F (433° C). In patients whose smaller vessels are so badly obstructed that the suction brings about only a slight increase in the circulation, and also in some sudden obstructions, as by thrombosis, it is safest to keep to temperatures about 90° F (322° C), and, if the temperature cannot be increased without causing pain to try further dilatation by use of drugs or nerve block. As observed by N E Freeman,7 local heat produces vasodilatation because the heat increases the local When the metabolism of the tissues arteries are normal, the increased need for nutriment is upheld by the augmented blood supply. However, when organic obstruction is present, the increased metabolism causes a more rapid utilization of whatever blood can enter the limb .- and, this amount of blood being already madequate, tissue starvation is increased. In this manner local heat may cause considerable increase in pain and may initiate or increase gangiene

F V Theis and M R Freeland's arc of the opinion that alternating pressure treatments primarily affect the oxygen-carbon dioxide exchange in the tissues regardless of whether or not circulation is increased. Skin temperature readings were taken with the Tycos dermotherm, and gas analyses of venous blood (obtained from the saphenous vein

or one of its branches in the upper part of the leg) were made by Van Slyke's manometric method. Vasodilatation as a result of direct heat or reflex heat was found more effective in increasing peripheral circulation than pressure treatments alone, but apparently has little effect in augmenting oxygen-carbon dioxide exchange in the tissues Combining reflex vasodilatation with pressure treatments proved of greater clinical value than either measure alone. The reflex vasodilatation produces maximum increase in the circulation, and the pressure treatments augment local tissue metabolism The respiratory function of the skin itself may be an important factor in the success of pressure treatments Proper care of the skin-keeping it soft and pliable by cleansing and greasingis of extreme importance, possibly aiding in absorbing oxygen from the air and eliminating carbon dioxide into the air

On the basis of a study of 18 arteriosclerotic cases presenting vascular symp toms of the lower extremities, J R Veal and W M McCord9 conclude that the oxygen saturation test does not offer an absolute standard as to prognosis in treatment of arteriosclerotic vascular disease of the extremities with the alternate suction and pressure method However, generally speaking, an increase in oxygen saturation of either the superficial or the deep venous blood, or an increase in both, after one hour trial treatment indicates that some improvement will follow this therapeutic procedure. When no change or a fall in oxygen saturation occurs after one hour trial treatment the prognosis is quite poor After treatment with alternate suction and pressure there may be a wide discrepancy between the changes of the oxygen content of the deep and the superficial venous blood

Intermittent Venous Compression—The value of intermittent venous

compression in the treatment of peripheral vascular disease has been brought to attention by W. S Collens and N D Wilensky 10 The efficiency of such treatment is based on the phenomenon of "reactive hyperemia"—the flush or hyperenia which develops during the release of obstruction of circulation of an extremity-described by Bier in the beginning of this century T Lewis and R T Grant (1925) demonstrated that during the release of venous congestion there occurs through active vasodilatation in the arterioles an increase in arterial flow of as much as 600 per cent depending on the degree and duration of application of venous congestion. Although the maximal increase in flow can be obtained by applying 90 mm of pressure for 15 minutes, Collens and Wilensky observed that patients suffering from organic arterial occlusion without ulcers or gangrene derived the best results with a pressure at levels of from 80 to 90 mm of mercury for alternating periods of two minutes for as much as 12 hours a day. After two weeks of such continuous treatment, treatment for periods of two hours three to four times a week, was employed. It has been necessary to continue these interval treatments in cases ot arteriosclerosis obliterans with evidence of ulcer or gangrene the greatest relief has been obtained with a pressure of from 40 to 50 mm of mercury for periods of one hour alternating with one hour of rest during the waking hours. In some of these cases if treatment was given continuously edema of the foot developed, which would disappear after the discontinuance of treatment for a day

The venous filling test described by Collens and Wilensky, 11 is useful in determining quantitatively any change in vascular capacity. "The test is performed by elevating the feet above the

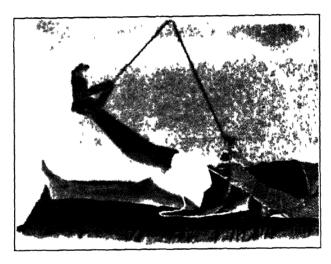
level of the head and moving the toes until the foot is blanched and the veins are collapsed. On placing the feet in the dependent position, the time is noted that it takes the veins on the dorsum of the foot to fill with blood. Since the lunar valves in the veins prevent a reflux of blood into the peripheral circulation, whatever blood enters the veins of the dorsum of the foot must obviously come from the arteries and through the capillaries. We have found that the normal venous filling time is from eight to ten seconds. In pathologic states the delay in venous filling is directly proportional to the degree of vascular obstruction" In some cases marked improvement in the venous filling time has been observed after the institution of treatment with intermittent venous occlusion 29 unselected cases this method of treatment proved capable of relieving pain, healing ulcers and increasing walking capacity

G de Takats, F K Hick and J S Coulter12 call attention to the fact that with every phase of suction in treatment by alternating negative and positive pressure there occurs a marked compression of the thigh and that all subjective and objective phenomena occurring during and after treatment by alternating negative and positive pressure can be reproduced more simply by intermittent venous compression. In four types of alternating suction and pressure apparatus, an intermittent venous stasis in the limb under treatment was observed. W Bierman4 pointed out as a defect in alternating suction and pressure the compression made around the leg by the cuft used to seal off the device in that it caused some embarrassment to venous circulation and to a lesser degree to the arterial circulation. It is not claimed by de Takats and his co-workers that the treatment by alternating negative and

positive pressure operates wholly on the basis of intermittent venous hyperemia, since in the suction pressure treatment there is without a doubt a partial release of the cutaneous vessels from atmospheric pressure and this vascular massage of the skin may have reflectoric circulatory effects on deeper structures

After careful study of the physiologic aspects of intermittent venous hyperemia, de Takats and his co-workers have adopted the following triphasic cycle in

venous compression is determined by the appearance of a definite rubor, which occurs in from one to two minutes when pressures of from 60 to 90 mm are used. Two minutes of compression should be followed by four minutes of release (three minutes in the horizontal position and one minute in the elevation position). When the circulatory embarrassment is more pronounced, one minute of compression will readily produce a rubor and is followed by one minute release



l ig 1— Apparatus in use. For the home, the pulley can be screwed into a door jamb, or a wooden traine can be constructed order Takats, Hick and Coulter (J. A. M. A., June 5, 1937.)

its application (1) elevation of the leg (2) venous compression (with a wide 8-inch cuft conically shaped to fit the thigh) while the leg is still elevated, and (3) horizontal position followed by release. When the leg is clevated the arterial pressure falls and also the venocapillary bed empties-making room for fresh blood. The amount of venous compression used varies between 90 and 60 mm of mercury in an extremity free from edema, cyanosis, ulceration and When the latter conditions gangrene are present, 40 mm of mercury should not be exceeded at first, although with later improvement the pressure may be gradually increased The duration of the and one minute elevation, a cycle of three minutes. Ordinarily 30 minutes of this vascular exercise in the morning and 30 minutes in the evening are prescribed. Should it prove uncomfortable, either the pressure or the duration of the individual cycle should be adjusted in order to obtain maximum benefit. When the patient is very sick, a relative or a nurse may inflate or deflate the cuff and lift the leg (Fig. 1).

The length of time the treatments should be continued has not been determined. In periods of stress, such as the spring and fall months, treatments are usually particularly indicated. Combination of intermittent venous hyper-

emia with methods that help to relax constricted vessels seems worthwhile Spreading infection, thrombophlebitis and widespread arteriolar destruction constitute the contraindications to the use of intermittent venous hyperemia

The ability to continue at home a type of exercise which opens and dilates the venocapillary bed as far as it will dilate is of importance in the patient's mental outlook The procedure is not a cure but merely a means of halting the progress of or slightly improving progressive obliterative disease of the peripheral arteries

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III DISSECTING ANEURISM OF AORTA

During the year just passed several groups of clinicians have reported cases of dissecting aneurism of the diagnosed correctly antemortem probable that dissecting aneurisms are even more common than pathologists realize, since in all likelihood some cases of sudden death-commonly ascribed to a "heart attack"—are of this nature

Unical and anatomical analyses of 13 cases, 11 males and 2 females, of dissecting aortic aneurysm directly related to the death of the patient and of six other cases found incidentally among 8200 necrousies of patients of all ages at the Massachusetts General Hospital have been made by R E Glendy, B Castleman, and P D White 1 In 2 of the 13 "acute" cases the diagnosis was made correctly during life. Pathologically, the predominant features of dissecting aneurism are (1) Intimal rupture near the aortic valve ring, (2) dissection of the medial coat of the aorta, and (3) some degree of medial degeneration Medionecrosis aortae idiopathica cystica (Erdheim) was present in nearly one-half (6) of the acute cases and in two of the six incidental cases of the series The lesion consists of focal, and occasionally fairly diffuse, mucoid or hyaline degeneration of the media which results in cyst formation or so-called "faults" The dissection lies almost always between the middle and outer thirds of the media involving about one-half or two-thirds of the circumference of the vessels. Syphilis was not an etiological factor in any case. At times proximal dissection involving the mouths of the coronary vessels occurs, and may cause confusion in differentiating dissecting aneurism and coronary thrombosis

As stated by T. M. Peerv,2 atherosclerosis does its greatest damage to the intima and the inner layers of the media, leaving the outer portionof the media and adventitia relatively uninvolved, whereas, syphilis usually does its greatest damage in the adventitia and the outer coats of the media with relatively little actual weakening of the intima, in spite of its altered appearance Thus, hermation of the inner coats through the diseased outer ones, with the formation of the saccular aneurism, is

the common thing in syphilis of the aorta, while a rupture of diseased inner coats and a dissection inside of healthy outer coats occurs in atherosclerosis

Dissecting aortic anemism occurs predominantly in males between 40 and 60 years of age in whom there is an antecedent history of hypertension Overexertion, either physical or mental, especially associated with hypertension, has been stressed as an etiological factor. The frequent location of the initial tear in the ascending aorta about 15 cm from the valve has suggested that the effect of the repeated diastolic recoil has etiologic importance.

Diagnosis—As discussed by Glendy, Castleman and White, the following features should point to correct diagnosis of dissecting aortic aneurism (1) Sudden onset of severe tearing or crushing pain usually thoracic, reaching its maxmum intensity at once, in a person with a history of hypertension, (2) wide and variable radiation of the pain to the head, back, abdomen, or lower extremities, or to all of these but rarely to the arms, (3) moderate to extreme collapse, and occasionally unconsciousness even though the blood pressure may be maintained for some time at a high level, (4) evidence of arrenal obstruction to the head extremities or kidneys (characterized by anuria) when dissection along the branches of the aorta has occurred, (5) a rapid enlarged heart with or without significant murmurs, (6) slight to moderate tever and leukocytosis (7) occasionally hoarseness when rupture has occurred into the mediastinum, (8) electrocardiographic findings which are not characteristic of coronary thrombosis, and, except in rare instances, (9) sudden death a few hours to a few days after the onset of the illness, as a result of rupture of the aneurism externally into pericardial sac, pleural cavity, mediastinum or elsewhere

Differential Diagnosis — Coronary thrombosis and peripheral arterial embolism, particularly of the iliac, cerebral or pulmonary vessels, are the two conditions most likely to be confused with dissecting aortic aneurism Points helpful in the differentiation from coronary thrombosis are (a) History of angina pectoris in most cases of coronary thrombosis, and rarely in those of dissecting aneurism, (b) the immediate, overwhelming pain in dissecting aneurism in contrast to the gradually developing pain of coronary occlusion, (c) the widespread location and radiation of the pain of dissecting aortic aneurism, often in or to the back, head, abdomen and to the legs, but rarely to the arms, which last mentioned radiation is commonly encountered in coronary thrombosis, (d) the frequent persistence of hypertension in the case of dissecting aneurism, (e) the evidence of very early obstruction of the arterial circulation to some part of the body other than the heart in cases of dissecting aneurism, and (f) the pathognomonic evidence of coronary thrombosis shown by daily electrocardiograms It is of interest that while three out of every four patients with coronary thrombosis survive the acute attack, only one out of every tour individuals with dissecting aortic anemism survives

The very severe pain in the thorax or abdomen, without much breathlessness the suddenness of the onset of trouble without previous evidence of disease of the heart or veins which might provide a source for embolism, and the commonly fatal course of the illness serve in most cases to distinguish dissecting aneurism from *embolism* of the illac, cerebral, or pulmonary arteries

Prognosis — Dissecting aortic aneurism of the "acute" clinical type is an

overwhelming illness, ending suddenly in death within a few hours or days Among the cases with rather extensive aortic dissection in Glendy, Castleman and White's series, only 1 in 14 recov ered completely. Among the acute cases, survival after the onset of symptoms averaged approximately four days, with three exceptions in whom the duration of life was 6, 8, and 15 weeks, respectively Rarely, when spontaneous rupture back into the lumen of the aorta or one of its large branches occurs, there is recovery with survival for months or years Among the incidental cases there was one patient who showed at autopsy a "double-barreled" aorta

Treatment-I he only rational medical treatment consists of keeping the patient absolutely quiet under opiates. D Gurin and his associates (1935) reported surgical treatment in a case in which the dissection extended into the right external iliac artery, involving one-third of the circumterence of the vessel on its lateral aspect and opposing the intimal surfaces so as to cause nearly complete obstruction to the flow of blood to the lower extremity. An undissected area of the vessel was meised and when the lumen was found so reduced by pressure from blood within the coats of the vessel the intima was also incised allowing the flow of blood from the dissected cavity back into the lumen of the vessel thus relieving the increased pressure from above within the vessel wall and restoring the circulation to the extremity which was maintained until death six days later. It is well to re member that in rare instances surgery may prove worthy of consideration

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IV. ANGINA PECTORIS

Medicinal Treatment \ study of the effect of different drugs on 26 patients with angina pectoris has been reported by J. E. F. Riseman and M. G. Brown 1. The efficacy of treatment was ascertained by the usual clinical methods and also by determining how much work, under standardized condinons, the patient could perform before pain developed. The exercise consisted of repeatedly mounting and descending a two-step staircase until precordial pain or discomfort developed. Control observations were made to differentiate between spontaneous remissions and improvement due to treatment. All patients were observed in a special clinic for from one month to one year before therapy was begun. Each drug was administered for at least one week before attempting to evaluate the results. When there was evidence that a drug had exerted a beneficial effect, the medication was discontinued and an mert tablet of similar appearance was substituted. The effect of medication was judged clinically by (1) the patient's own estimation of the efficacy of the drug (2) the actual number of attacks experienced or the actual number of tablets of glyceryl trinitrate required during the period of medication and (3) the occurrence of untoward or unexpected symptoms

The patients estimation of therapeutic benefit indicated that all the drugs were approximately equal in value placebos were just as often beneficial as other medicaments. (This finding is in agree ment with the observation of H. Gold, N. I. Kwit and H. Otto in a clinical study of the observation and animophylline discussed next—L.D.: However, the exercise tolerance test revealed that patients whose treatment consisted of lactose, sodium bicarbonate, potassium

iodide, or tissue extract were unable to perform any more work than was possible without medication

Glyceryl trinitrate administered before work was undertaken prevented attacks and enabled many patients to do considerably more work. This prophylactic effect was often of relatively short duration, but attacks were prevented for as long as one hour in many instances. Such individuals could be rendered completely free from attacks in daily life by taking glyceryl trinitrate at hourly intervals. For all practical purposes, small doses (½000 grain or 0.1 mg) were as valuable as larger doses and were attended by little discomfort.

One-half of the patients were benefited by aminophylline or by quinidine sulfate. Ammophylline had to be given in doses of 3 grains (0.2 Gm) to be effective Theophylline calcium salicvlate, erythrol tetranitrate atropine sulfate were often of value. occasionally benefiting patients not helped by other aminophylline or quinidine sulfate The doses of atropine necessary frequently caused discomfort because of Codeine sulfate and side-reactions phenobarbital raich enabled the individual to do more work before pain developed, but these sedatives appeared to be of aid as an adjunct in the treatment Sodium nitrite and small doses of dinitrophenol were only rarely of benefit Dinitrophenol, even in the small doses used, 112 gr or 100 mg daily, occasionally gave undestrable side-reactions Digitalis rarely proved of value, and frequently caused a striking increase in anginal attacks

The effect of *theobromine* and *amino-phylline* on cardiac pain has been studied by H Gold, N T Kwit, and H Otto² in a group of 100 ambulant patients with angina pectoris. The patients were selected on the basis of proof of organic

TABLE 1
CHANGES IN PAIN DURING FIRST COURSE OF
TREATMENT

| Number of Patients | Theo- bromine | Placebo |
|--|--|---|
| Pain unchanged Pain diminished Pain increased Duration of course | 63 22 15 1 6 weeks (1-4 weeks) | 69 25 6 2 6 weeks (1-8 weeks) |

heart disease, cardiac pain on effort, little or no physical work and faithful cooperation. An attempt to include only patients who could distinguish relief afforded by glyceryl trinitrate from relief by a soluble placebo tablet taken in the same way during an attack of pain was abandoned, because a fairly large number of patients with cardiac pain were found who could not distinguish between the two-which fact is due to the transient character of effort pain in a large proportion of the individuals. The effect studied was the influence on the severity and frequency of the attacks, and on the capacity for effort without pain - not relief during attacks of pain. The data consisted of the patients' judgments regarding changes in pain, secured in a manner as relatively free of bias and personal judgment as possible

In all, 209 courses of treatment with the *xanthines* were given, each course being alternated with a course in which a placebo of lactose (or some other agent) was used *Theobromine* in the form of a 5-grain (0.3 Gm.) tablet was used in all the cases, and in 12 of them tests with *aminophylline* (theophylline with ethylenediamine), given in $1\frac{1}{2}$ -grain (0.1 Gm.) tablets, were also made. The total dose of theobromine varied from 15 to 60 grains (1 to 4 Gm.), given in single doses of from 5 to 15 grains (0.3 to 1 Gm.), at intervals of about six hours. Daily dosage of *theobromine*

| TABLE 2 | | | | | |
|---------|-------------|-------|----------|-----------|-------------|
| THE | COMPARATIVE | VALUE | AND COST | OF PURINE | DERIVATIVES |

| Processor the holdings of the process of the proces | , | ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,, | | |
|--|--|--|--|--|
| Preparation and Dosage* | Total Patients Bene- fited, per cent | Patients Showing 50-100% Increase in Exercise Tolerance, per cent† | Frequency of Gastric Distress, per cent | Cost per 1000 Doses Dollars |
| Theophylline with sodium acetate, 2½ grains Theophylline with sodium acetate, 7½ grains Theophylline with calcium salicylate, 8 grains Theophylline with ethylenediamine, 3 grains Theophylline, 3 grains Theophylline, 3 grains Theophylline mono-ethanolamine, 3 grains Theophylline with methylglucamine, 2½ grains Theophylline with sodium salicylate, 7½ grains Theobromine with sodium salicylate, 7½ grains Theobromine, 5 grains | 80 77 67 59 56 54 54 45 34 | 27 24 13 12 19 7 9 0 0 | 13 18 27 30 13 13 13 9 9 | 26 25‡ 5 00 32 00\$ 21 00\$ 32 00\$ 6 55 36 00\$ 16 60\$ 3 85 3 16 |

^{*} Each preparation was given four times a day, on crising after linch after supper and before retiring

varied from 15 to 60 grains +1 to 4 Gm), and the daily dosage of aminophylline from 9 to 12 grains (06 to 0.8 Gm i given in single doses of 3 grams (0.2 Gm), three to four times a day The xanthines were given in courses lasting from 1 to 25 weeks, the average being 312 weeks. The effect on cardiac pain of the first course of treatment with the xanthines was compared with that of the first course of a placebo (Table 1) Every type of change in pain observed during the use of a xanthine was reproduced in the same individual by a placebo Most of the patients reported no change, a small number reported that the pain was worse, and about one-fourth of the patients in each group reported improvement. The results show, therefore, that patients with cardiac pain are unable to distinguish the effects of a placebo from those of a xanthine when measures are taken to preclude the identification of the agent by any means other than the relief of pain. The conclusion is drawn that the **xanthines** exert no specific action which is useful in the routine treatment of cardiac pain.

Clinical reports on the xanthines in cardiac pain are inclined to be based on the results of the studies with the isolated heart and in ane-thetized animals, which show fairly consistently that these drugdilate coronary arteries. The bias created by the emphasis placed on the clinical significance of the experimental results is undoubteelly responsible at least m part for the fact that the question whether the xanthines actually relieve cardiac pain in patients with coronary disease has received so little satisfactory independent examination. Exception to the general belief regarding the efficacy of the xanthines in angina pectoris has also been taken by W. Evans and C. Hoyle, who in a study of 90 patients were unable to convince themselves that the xanthines- as well as the other

[†] Great improvement

[#] The cost of these preparations is based on the prices published in the catalogues of the pharmaceutical houses

^{\$} These represent the cost per thousand doses of the medication in tablet or capsule torm as prepared by the pharmaceutical houses. All other costs are based on the price per pound of powder plus the cost of manufacturing tablets.

drugs which were tested-are worthy even of trial in the routine treatment of cardiac pain

Comparative Value of Purine Derivatives—The comparative value of six theophylline, four theobromine, and one caffeine preparations has been studied by M G Brown and I E F Riseman⁴ in 17 patients with angina pectoris, by the usual clinical methods and also by the standardized exercise tolerance test The optimum dosage was (1) usually the maximum amount that could be given without causing severe gastric distress. Not all individuals responded to purmes The sodium acetate derivatives of theophylline and theobromine were found to be the most effective preparations (Table 2) who did not respond to these drugs usually derived benefit from the theophylline with calcium salicylate, which was the next best preparation

Theophylline, theophylline with ethylenediamine, theophylline monoethanolamine, theophylline with methyl glucamine, and theobromine with calcium salicylate were about equally effective, but were less so than the aforementioned preparations. Theobromine and theobromine with sodium salicylate were distinctly less effective, while caffeine citrate was of Sedatives are of value little or no value in the treatment of angina pectoris, but their combination with the purme does not result in an increased exercise tol-Theobromine with sodium crance acetate is by far the least expensive of the effective purine preparations

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V. CORONARY ARTERY DISEASE

1. Coronary Disease in Youth

In recent years it has become recognized that disease of the coronary arteries may occur in individuals of early middle age and even in youth A clinical analysis of 100 patients under 40 years of age with unquestionable coronary disease, by R E Glendy, S A Levine, and P D White,1 has shown that approximately 17 per cent of all coronary disease occurs in individuals under 40 years of age The ratio of men to women in this younger age group is 24 1 (about six times greater than encountered in general) Hypertension is an important factor in youth, predominantly in women A greater number of voung patients than of patients in general may be expected to have hearts that are normal in size Fewer complications are encountered. diabetes or evident peripheral vascular disease is uncommon. The duration of life for those who died and the life expectancy of the survivors is greater than for patients of all ages with coronary disease, but the susceptibility to sudden death is just as great

Comparison of the mode of life of the 100 patients with coronary disease with that of 300 healthy old men and women living at ages past 80 years revealed that inheritance and ancestral longevity are important factors in the early occurrence of coronary disease. Relatively far more (90 per cent) of the old folks than of the young group with coronary disease were of British stock (but selection and other factors, such as time of immigration, may well enter here) In the older group there were no persons of Jewish extraction, whereas 39 per cent of the young group were lewish Urban life, sedentary occupations and habits, possibly excesses of diet, the excessive use of tobacco, overweight, and increased nervous sensitivity and strain all appear to be more predominant on the part of young patients with coronary disease than among individuals who have achieved long life. Serious intections and alcohol seemingly do not play an important role

2. Factors and Events Associated with Onset of Coronary Thrombosis

Although both angina pectoris and coronary thrombosis have the same underlying pathologic condition, viz, coronary sclerosis, they apparently differ in respect to the exciting cause of the attack statistical study of 817 attacks of coronary thrombosis, occurring in 555 patients has been made by A. M. Master, Dack, and H L Jaffe? in order to determine what factors may initiate thrombosis Coronary thrombosis occurs in all walks of life and all types of occupations. Exertion, even severe, is of little or no significance in the precipitation of an attack. Excitement ingestion of food infection tobacco alcohol heart failure. time of day, and season of year were found to have no significance. The effect of operation and of insulin require further study

Angina pectoris is a functional syndrome which appears when there is temporary insufficiency of coronary blood flow as a result of exertion or reflex spasin—the nervous element being paramount. Although some attacks of angina pectoris occur without discernible cause the majority are definitely related to specific acts, such as excitement, walking against the wind cating a nical or playing golf, and the attack is relieved by glyceryl trinitrate. Coronary thrombosis, on the contrary, occurs irrespective of rest activity, excitement or emotion and

season or temperature, and is not helped by glyceryl trinitrate. Physical and mental rest are of importance in the treatment of coronary artery disease, but thus far medicine has been unable to prevent the formation of a thrombus

3. Preliminary Pain in Coronary Thrombosis

Fifteen cases of coronary thrombosis with mild anginal attacks preceding the clinical picture of thrombosis by hours or days (usually from 12 to 48 hours) have been studied by H. Feil. The preliminary pain was not dependent on effort or emotion, was more or less continuous and of an oppressive and burning character. In two of five patients on whom electrocardiograms were taken during the preliminary pain, the findings were normal, in three cases the curves showed slight changes in the height or contour of the T-waves, but the changes were not uniform gradually forming thrombus in a stenosed coronary artery appears to be the most probable explanation for the preliminary pain. The possibility of the development of a coronary artery thrombus should be suspected in individuals who have persistent retrosternal pain, not related to effort, emotion or digestion, especially when hypertension or the anginal syndrome has been previously noted. Urging of fluids (to avoid dehydration). administration of aminophylline, alcohol and nitrites, moderate restriction of physical activity mental rest restriction of tobacco and insulin are indicated effort being made to improve coronary artery flow

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- 2 Mister A M Dick S and latte H I I A M A 109 546 (Aug 21) 1937
- 3 Feil H Am J M Sc 193 42 (Im) 1957

VI. ELECTROCAR-DIOGRAPHY

1. Prolonged Q-T Interval in Electrocardiogram

R Hegglin and M Holzmann¹ have observed a lengthening of systole regularly in hypocalcemic conditions, such as tetany, hepatic coma and uremia, and as the calcium content of the blood serum increased it was reversible Under toxic influences and metabolic and endocrine disturbances, the lengthening of the Q-T interval signifies a grave condition, but the prognosis is not entirely unfavorable In hypertrophied hearts in hypertension, and in the early and late stages of myocardial infarction, a slight prolongation of the Q-T interval is relatively frequent as a manifestation of a longer lasting stimulation in the pathologic portion of the heart. The lengthening of the Q-T interval, which occurs in pulmonary embolism and in collapse-like and comatose conditions, remains unexplained in regard to its mechanism and significance In hypocalcemia the total process of excitation is abnormally prolonged, whereas m the other groups with Q-T lengthening, it is chiefly the retrogressive phase that is abnormally long

Prolongation of ventricular systole as measured from the beginning of the O-wave to the end of the I-wave of the standard electrocardiogram has been demonstrated by P. S. Barker, F. D. Johnston, and F. N. Wilson² in nine patients with abnormally low blood serum calcium levels. Duration of mechanical systole, as measured in heart sound records, is not prolonged in hypocalcenia.

2 Chest Leads: Normal Variations

In a study of 150 normal individuals (50 adults and 100 children), the normal variations of chest lead electrocardiograms have been described by

E. Sorsky and P. Wood.³ For the apexleft leg lead (the electrode being arranged so that relative negativity of the exploring electrode produces an upward deflection on the electrocardiogram) normal appearances include the following

- 1 A small, frequently inverted P-wave, which may however be upright, biphasic, or isoelectric
- 2 A biphasic QR complex which may be nearly all Q or nearly all R according to the position of the exploring electrode An extra initial upward deflection may sometimes occur Notching or slurring of any portion of the waves is common
- 3 The R-T take-off is usually isoelectric but may be depressed to a maximum of 2 mm, or rarely may be slightly elevated
- 4 There is commonly no appreciable isoelectric period of the R-T component unless the T-wave is small, biphasic, or upright
- 5 The T-wave is usually sharply inverted and of considerable amplitude. Under certain conditions, especially in children, it may be upright or biphasic, according to the position of the exploring electrode. One T-wave measured 15 mm in amplitude, and there were several over 10 mm. There was no reason to suppose that these large T-waves were abnormal.
- 6 Within certain limits shift of the exploring electrode to the right yields a relatively smaller Q-wave, a relatively larger R-wave, and a less inverted T-wave, shift of the exploring electrode to the left has the opposite effect (Fig 2)

In a special study of 86 school boys, an upright T-wave in the left pectoral-left leg lead tended to be associated with small or with pendulous hearts, or with hearts characterized by an exaggeration of the pulmonary arc, whereas a T-wave which remains inverted in the right pectoral-left leg lead tends to be associated with relatively large hearts or with transverse hearts associated with high dia-

phragms If this be true, T should be inverted in the right pectoral-left leg lead in hypertensive heart disease and in aortic valvular disease, and should be upright in the left pectoral-left leg lead in mitral stenosis and in heart disease secondary to emphysema. The three fattest boys showed an inverted T-wave in the right pectoral-left leg lead, which change was shown by no slim boys. The tendency toward upright T₄-waves in

standard electrocardiogram in hypertension with left ventricular hypertrophy shows. (1) Moderately high voltage, (2) left axis deviation, (3) inversion of T₁, and (4) a tall, upright T₃. In this type of heart disease, when the outermost border of the left ventricle extends to or beyond the anterior axillary line, a chest lead taken with the exploring electrode (RA) at the apex is really an axillary lead and not a left pectoral lead.* Axil-

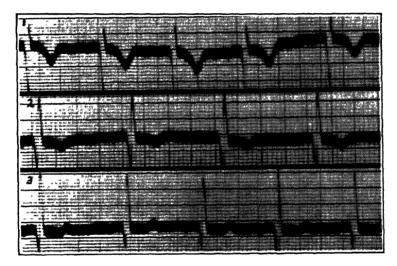


Fig. 2—Showing the effect of shifting the exploring electrode. 1. Apex—left leg lead. 2, left pectoral—left leg lead. and 3, right pectoral—left leg lead. (Sorsky and Wood. Act Heart I. Feb. 1937.)

children with thin chest walls and narrow thoracic cages has been called to attention also by M. Robinow, L. N. Katz and A. Bohning 4

In view of the difficulty of fixing the exploring electrode in a constant position in regard to the underlying heart great caution must be exercised in the interpretation of serial chest lead electrocardiograms.

3 Chest Lead Tracings in Hypertension

A possible source of error in the interpretation of chest lead tracings in arterial hypertension with cardiac enlargement is called to attention by I. R. Roth b. The lary leads in normal individuals resemble standard limb leads—the axilla-foot lead resembling standard Lead III. Consequently, apical chest lead tracings in cases of this type present an aprophit I-teat (Fig. 3), which may lead to confusion it an attempt is made to evaluate such a tracing unconditionally in the light of citeria established for normal apical chest lead tracings

4 Absent or Small Initial Positive Deflection in Precordial Lead

In an analysis of electrocardiograms obtained in 4500 consecutive patients at

^{*} Exploring electrode pri ed malway between the sterning and male regular line

the Mount Smai Hospital, New York City, by A M Master, 5 Dack, H H Kalter and H L Jaffe, 7 the initial positive deflection in the precordial lead (Q-wave of old, R-wave of new technic) was absent in 120 (27 per cent)

a wave directed downward, and negativity by a wave directed upward, the opposite of that which obtains in the standard leads. The precordial electrocardiogram obtained (Fig. 4) consists of an initial downward positive deflection (Q-wave)

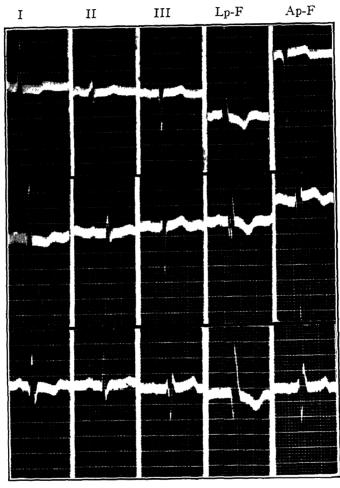


Fig. 3—Standard Leads I. II. III. and chest leads. Lett pectoral-Loot (IpF) and Apex-Loot (IpF). L.B. and C represent cases of arterial hypertension with cardiac enlargement. In each case I, shows inversion of its first portion, and T_1 is upright. The LpF chest lead shows a negative T wave (normal pattern) and the IpF chest lead shows an upright or partly upright. I wave resembling in general standard Lead III. (Roth. Am. Heart J. Aug. 1937.)

and was small (2 mm or less) in 175 (39 per cent). The chest lead was taken by placing the right arm electrode over the precordium just within the apex, in the fourth or fifth interspace, and the left leg served as the site of the indifferent electrode. By this method positivity of the precordial lead is represented by

followed by an upward negative deflection (R-wave), the T-wave is inverted

In 64 patients, the precordial lead was studied with the precordial electrode placed in five different positions on the chest wall Position1 was two centimeters to the right of the right sternal line in the fourth interspace, position 2, in the

midsternal line, position 3, two centimeters to the left of the left sternal line in the fifth interspace, position 4, just within the cardiac apex; position 5, outside the apex. In these 64 patients, the "neutral point" or "zero potential" method described by F. N. Wilson and coworkers, was also employed to determine if it possessed any practical advantage over the old procedure.

In two-thirds of the patients with absence of the initial positive deflection, it

in the routine position (just within the apex), precordial leads obtained from other positions on the chest wall usually demonstrated absence of the initial positive deflection (Fig. 6). This holds frequently when a large initial negative deflection precedes a large positive deflection. All the individuals with this abnormal type of QRS had marked myocardial disease, 15 of the 24 had suffered a coronary occlusion. The frequency of such a QRS group in patients with

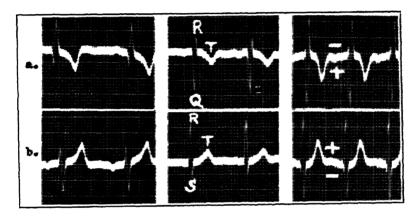


Fig. 4—Three examples of normal precordial lead. (a) Recorded in the customary manner so that negativity of the precordial electrode is represented by an upward deflection. The old nomenclature is given—in initial downstroke Q followed by the intrinsic deflection R. In the third example there is a small initial upward deflection preceding the Q. The F wave is inverted (b) Recorded so that negativity of the precordial electrode is represented by a downward deflection. New nomenclature—an initial upward deflection R and an intrinsic deflection S. In example three there is a small Q. The T wave is upright. (Master, Dack, Kilter, and Taffe.) Am Heart I. Sept. 1937.)

was associated with recent or old coronary thrombosis and anterior wall intarctions (Fig. 5) in one-fifth with coronary artery disease alone with or without hypertension (possibly cases of unrecognized invocardial infarction) and in the remaining 14 cases the (hagnoses were miscellaneous, 712) acute and chronic glomerulonephritis rheumatic and syphilitic valve disease pincumothorax, Graves disease, and acute invocarditis—all without evidence of myocardial infarction

In 24 patients presenting M or W-shaped QRS complex with the electrode

block had been pointed out previously by A Bohning and I. A Katz T. T. A Wilson and his coworkers to 11 concluded that an M or W-shaped QRS appears when only the inner layers of the centricular wall are infarcted, or when the precordial electrode is placed over the edge of an area of infarction. When the electrode is moved toward the center of the infarct the QRS will become of the usual type with a small negative deflection.

Absence of a small initial positive deflection in the precordial lead was

permanent in the majority of cases, even when an abnormal T₄ and abnormal standard leads returned to normal. Absence of the initial positive deflection was accompanied by an abnormal T₄ (one of negative polarity—upright T-wave of old terminology) in 54 per cent of cases; nearly all (82 per cent) were cases of coronary thrombosis While myocardial involvement was present in all of the 46 per cent of the 120 cases

age. Bundle branch block occurred in 11 per cent, and a definitely enlarged heart in over one-half of the cases. In only one-fifth of these patients was there an associated abnormal T-wave in the precordial lead (in contrast with an incidence of 54 per cent in patients with an absent deflection). It was found that nearly all the patients with a small initial positive deflection and no evidence of heart disease had an intrinsic

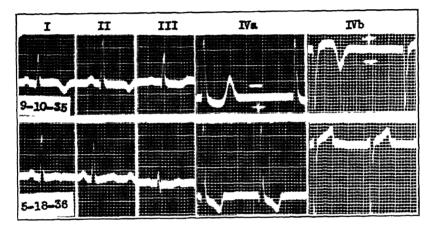


Fig. 5—Acute coronary thrombosis (anterior wall infarction). Male, aged 40 years. Sept. 10, 1935. One week after the attack. The standard leads show coveplane T_1 and T_2 . In the precordial lead the T-wave is directed oppositely to the normal and the initial positive deflection is absent. This is the typical appearance in anterior wall infarction. May 18–1936. The standard leads are returning to normal although T_1 is still semi-inverted. The semi-inverted and the initial positive deflection has reappeared but is small. This small deflection may be the only remaining abnormality following coronary occlusion. (Master, Dack. Kalter and Jaffe... Am. Heart J., Sept. 1937.)

with a normal T-wave, only nine had infarction

One hundred seventy-five (3.9 per cent of the 4500 patients) presented a small initial positive deflection (2 mm or less). In only 13 of the 175 patients (7.5 per cent) was the heart presumably normal, the remainder suffered from coronary thrombosis (29 per cent), coronary artery disease with or without hypertension (37 per cent), rheumatic valvular disease (14 per cent), miscellaneous heart involvement (12 per cent). Eighty-four per cent of these patients showed abnormalities in the three standard leads indicative of myocardial dam-

deflection measuring not more than 10 mm, while the patients with coronary thrombosis usually had a large intrinsic deflection in the presence of a small initial deflection. In view of this observation, the significance of the small initial deflection is greater when the amplitude of the succeeding deflection is above 10 mm. For example, an initial positive deflection of 15 mm appears to be less significant when the intrinsic negative deflection is 7 mm, than when it is 17 mm.

In 128 patients with infarction of the anterior surface of the heart, diagnosed electrocardiographically ($Q_1 T_1$ type) or

at autopsy, the initial positive deflection was absent in more than one-half, small in one-sixth, and normal in one-third (Tyble 3). In 78 patients with infarction of the posterior wall (Q₃ T₃ type), this deflection was rarely absent, but was frequently small. In 30 patients

surface of the heart was damaged. A small deflection, however, occurred almost as frequently in posterior as in anterior wall infarction. It is the opinion of the authors that a small initial posttive deflection is almost as significant as an absent one. In 26 patients with a

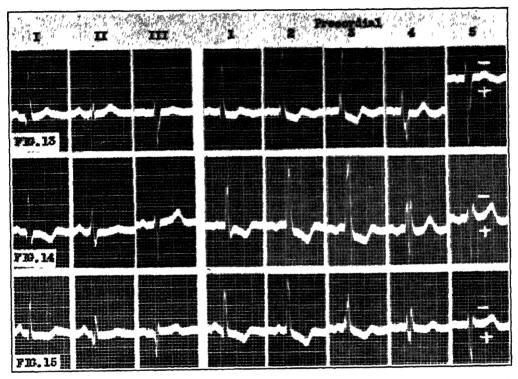


Fig 6—(Top)—Cononary thrombosis two years previously (anterior wall infarction). Male aged 49 years. Standard leads present residual Q₁ and W shiped QRS in Lead II. The QRS complex in the routine precordial lead (position 4) is of an abnormal type (R-S type) and the T wive is directed opposite to the normal. Other positions (1-2-3) show absence of the initial positive deflection. (Center)—Coronary thrombosis two years previously (interior will infarction). Male aged 59 years. Standard leads show Q₁. T₁ pattern. The QRS in the routine precordial lead (position 4) is M-shaped and the T wive is opposite to the normal. In positions 1-2 and 3 the initial positive deflection is absent. (Bottom)—Coronary thrombosis two years previously (posterior will infarction). Male aged 49 years. Standard leads show Q₁. Pattern Routine precordial lead (position 4) shows M shaped QRS, and an absential I wive. The initial positive deflection is absent in positions 2 and 3. (Master, Dack Kidter, and Title.) Am. Heart (Sept. 1937.)

with signs of infarction of both anterior and posterior surfaces, no clear-cut division was found, the initial positive deflection was normal small or absent, depending apparently upon which lesion exerted the predominant effect. If ith but two exceptions an absent initial positive deflection in coronary thrombosis occurred only when the anterior

small initial positive deflection, invocatdial infarction was found at autopsy in 15 instances, only one case showed normal heart muscle

Comparison of the old method of recording the precordial lead with the "zero potential" method of Wilson revealed no practical advantage of the latter as far as diagnosis was concerned

Total

| Location of Infarction | Number | Initial Positive Deflection | | |
|---|-----------------------|--|---|---|
| | of Cases | Absent | Small | Normal |
| Anterior wall Posterior wall Anterior and posterior Undetermined location | 128 78 30 25 | 71 (55 0%) 2 (25%) 9 (30 0%) 0 | 19 (15 0%) 9 (11 5%) 13 (43 0%) 10 (40 0%) | 38 (30 0%) 67 (86 0%) 8 (27 0%) 15 (60 0%) |
| Total | 261 | 82 (31 0%) | 51 (19 5%) | 128 (49 0%) |

TABLE 3 THE INITIAL POSITIVE DEFLECTION IN CORONARY THROMBOSIS (261 CASES)

(This procedure consists of pairing the precordial electrode with a central terminus which is connected through three large and equal resistances to both arms and the left leg, whereby any possible effects of the indifferent electrode are supposedly excluded)

5. Serial Changes in Lead IV

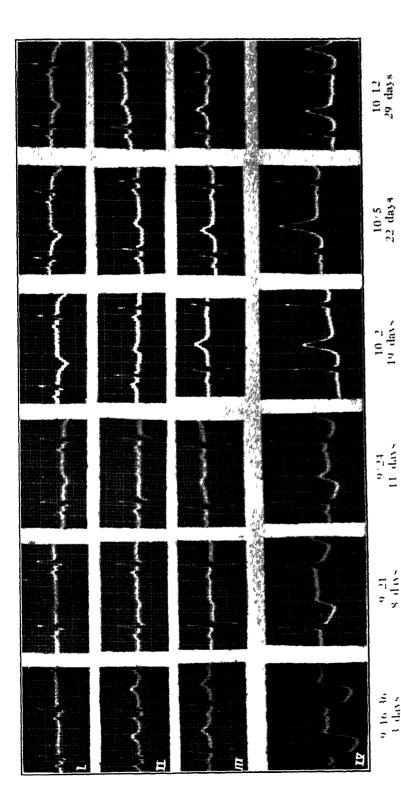
A study of the serial changes in Lead IV has been made by M. A. Feinstein and A. Licberson¹² on 12 patients (11 males and one female) diagnosed acute coronary thrombosis in Beth Israel Hospital. New York City None of the patients had received digitalis for weeks prior to or during the study. In taking the chest lead the anterior electrode was placed in the fourth interspace, 6 cm to the left of the midline and the indifferent electrode was attached to the left leg-Lour cases showed typical 'anterior" type of serial change four "posterior" type and the remaining four were of the indeterminate' type In anterior intarction the RS-T segment is at first depressed, and after this returns to normal, the Q-wave becomes smaller and the T-wave more upright, soon the classical picture of anterior intarction being shown, riz, absent Q4, and upright, coved T-wave (Fig. 6)

Posterior infarction shows at first a markedly elevated RS-T segment in Lead IV After this returns to normal,

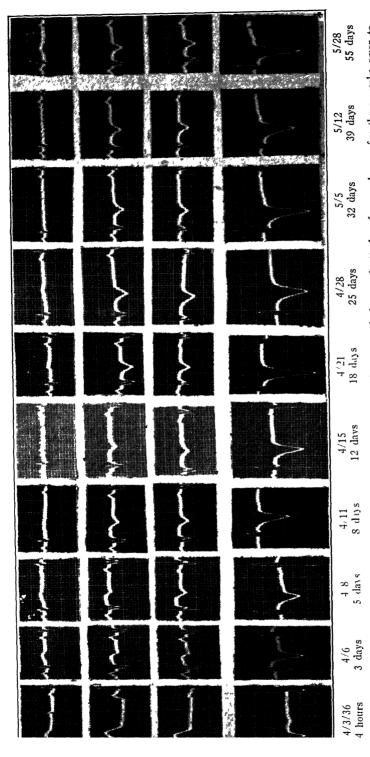
 Q_4 becomes large and T_4 is unusually deeply inverted (Fig. 7)

As in the conventional leads, the RS-T segment changes are likely to be the earliest ones, the markedly coved, sharply peaked or tall T-waves are more characteristic of the midperiod (the first three to four weeks) The changes characterizing the late stage of coronary thrombosis, and which appear to be permanent in a good many cases, are the abnormal form of the ORS and the direction of the T-wave. The change in O4 (either very deep in posterior infarction or absent in anterior infarction) is often among the first to appear and the last to disappear. Three or four months after the infarction there is little serial change in Lead IV

Occasionally a patient will not demonstrate a characteristic pattern of senal changes in the convential leads and will do so in the chest lead. If electrocardiograms are taken sufficiently early, the presence of a posterior infarct is registered in the fourth lead as is an anterior Particular emphasis should be laid on any tracings showing an elevated RS-T segment or a disproportionately deep negative T4 wave (often seen in posterior intarction) Lases of coronary thrombosis, presenting electrocardiagraphic changes fitting readily into the classical types described, seem to have better prognoses than the indeterminate



depression becomes less pronunent the I wave becomes constantly more positive. Quis absent throughout The upright The first trading (September 16) was taken three days after a single attack of persistent dull substernal burning. While the conventional leads show only a flat I-wave in Lead I with a suggestion of a Qrawave the RS-1 segment in Lead IV is strikingly depressed. As this RS-T It was ear unusually tall teven higher than the QRS on October 5) and indicate the presence of an active cardiac process. The till I-wave becomes smaller in time. The final (permanent) picture is apt to be an absent Qa wave and positive Is were. The conventional leads in this case also show serial changes (inversion of Ti), these changes at first are not as marked in I ead I as in I ead IV and are not as characteristic of acute coronary thrombosis. In Lead IN the sent delenges by meels into the americar infarct pattern from the start (Feinstein and Lieberson Anterior infarction 1 B No 86585 male aged 63 years Heart July 1937) 1 1g 7



he first electrocardogram (April 3, 1936) taken tour hours after the attack shows a markedly elevated RS-T segment in Lead IV. The T-wave is ad goes through a period when it appears almost normal (April 8 1936) except for the raised RS-T segment—a finding much more significant than sproportionately large in relationship to the relatively small QRS. The deeply inverted T-waves of April 21 and May 5 are very suggestive of an egative and already sharply pointed. Note the general similarity in contour of Leads IV, III, and II, and the dissimilarity to Lead I. The fourth similar depression in this lead. The T-wave later (April 11, April 15) becomes suspiciously asymmetrical (cove-planed) in shape, it is already No 81826 male, aged 45 years. The patient had several attacks of anginal pain for three weeks prior to An angmal attack of unusual severity, not relieved by nitroglycerine or morphine, one hour before admission brought him into the hospital ute process in the my ocardium. In the conventional leads the changes are typical of the Q3T3 type (posterior infarction). Fig 8-Posterior infarction M M

ation revealed no new abnormal findings. The electrocardiogram taken the next day (May 28) shows only the slight serial change predictable from This lack of electrocardrographic evidence of a new coronary closure in the conventional and the fourth leads helped the inicians decide that the most recent attack of precordial fain was probably anginal in nature and not due to a new infarction (Feinstein and Lieber-The patrent was discharged on May 17 1936, and readmitted May 27, 1936, because of recurrence of precordial pain and dyspnea Physical exami-Am Heart J, July 1937) ie previous infarction

type with small, slowly developing, atypical changes,-possibly because the infarction is single and not large.

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VII. EMBOLISM

Pulmonary Embolism

Death from pulmonary embolism is a much greater menace in both medical and surgical cases than is generally realized Factors which predispose to the occurrence of pulmonary embolism have been called to attention by A. R. Barnes¹ of the Mayo Clinic Females are more likely to die from this condition than are males. Obesity definitely predisposes to fatal pulmonary embolism. Age is a factor of conspicuous importance, the incidence being greater after 40 years of age Certain operations are followed by high incidence of pulmonary embolism, as much because of the late average age of the patients as because of the type of operation. Hermotomy, which is performed usually after the patient has passed the age of 40 years, is followed by a much higher incidence of fatal embolism than is appendectomy which

15 performed when patients are much younger on the average Most cases of fatal pulmonary embolism following surgical procedure are associated with abdominal conditions. In a high percentage of cases, history of malignancy 15 present Death from pulmonary embolism following thyroidectomy is almost never encountered, in spite of many instances of severe cardiac damage found among such patients

Cardiac disease is an outstanding predisposing factor. A crucial defect in the circulation, relating to formation of thrombi and resultant pulmonary embolism, consists of a reduced rate of venous blood flow, particularly in the "Normal venous circulation is maintained by a 21s a tergo of the systemic arterial circulation, which depends upon the maintenance of adequate systemic blood pressure, by contraction of the skeletal muscles, which presupposes activity of the muscles, by negative intrathoracic pressure, which results from normal respiration, and by the plunger-like action of the liver secondary to respiratory movements, tending to squeeze the blood out of the intra-abdominal venous channels these mechanisms are likely to be disturbed following operations on the abdomen. The blood pressure is prone to fall after operation, especially if the heart is damaged, movements of the legs are reduced and respiration is likely to be shallow and in consequence the excursions of the liver are diminished."

In eardiac insufficiency the circulation time is prolonged, the velocity of the venous return is reduced, and the veins of the lower extremities are the first to suffer when the circulation lags in the platelet count following operation, coincident with the period of anticipated embolism, has been demonstrated jury to the lining of a blood vessel favors

the localization and development of a thrombus Correction of the circulatory defect would seem to be the easiest way in which to break this chain of circumstances

The commonest situations of the thrombi in order of frequency are the iliac vein, the femoral vein, the pelvic veins, the prostatic venous plexus, the vena cava, and the right auricle Although pulmonary embolism is seen in

Not only may the classic symptoms of pulmonary embolism be lacking, but bloody sputum, pleural friction rub, or signs of pulmonary consolidation may not be present for 24 hours after the onset, and in some cases they are never present. When the embolism is massive but still sublethal, acute dilatation of the right ventricle and pulmonary conus (acute cor pulmonale) may occur. Increased pulsation may be noted in the

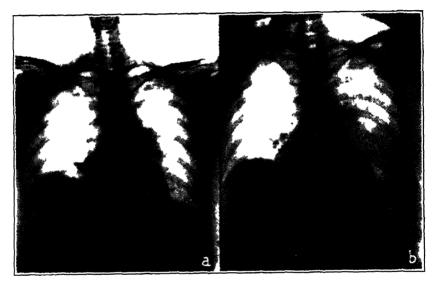


Fig. 9—a early stage of pulmonary embolism involving the left lower lobe increased hilus shadow on the left due to dilated vessels dulness at left base b four days later increased dulness at left base due to intarction and secondary pleural effusion—persistence of increased hilus shadow—Necropsy showed an embolus in the left pulmonary artery with infarction of the left lower lobe and left pleural effusion—(Baines—I. A. M. V. Oct. 23–1937.)

cases of thrombophlebitis, there is little evidence that the pulmonary embolism arises from the thrombus of the thrombophlebitis. Mild premonitory attacks not infrequently precede the tatal seizure

Diagnosis — Cyanosis and dyspica are usually looked upon as the cardinal signs of pulmonary embolism. It is important however, to regard as a common picture of acute pulmonary embolism, shock, with or without dyspinea, with faintness, pallor, sweating, acceleration of the pulse, a marked fall in blood pressure, voniting, and sometimes collapse

second and third interspaces to the left of the sternum. A loud systolic murmur may be observed in this region with marked accentuation of the second pulmonic sound and possibly a friction rub. Occasionally gallop rhythm, best heard to the left of the sternum, is present. The veins of the neck may be dilated and pulsating. In severe cases cyanosis of extreme degree may be present. In the early stages roentgenographic evidence of pulmonary embolism may be lacking. Accentuation of the hilus shadow on the side of the occlusion due

ELECTROCARDIOGRAPHIC DIFFERENCES IN ACUTE PULMONARY EMBOLISM AND IN ONE TYPE OF ACUTE CARDIAC INFARCTION

Type of Electrocardiogram Characteristic of Acute Pulmonary Embolism

S_t constantly present and usually prominent

S-T2-Take off usually below zero level

T₂ diphasic, monophasic, or upright rarely inverted

R-T, occasionally slightly elevated

T, inverted, may be cove-plane

 Q_i frequently fairly prominent, Q_i pattern not present

O, usually within normal limits

T, usually upright, may be flat or diphasic

Tx Type of Electrocardiogram, Characteristic of Acute Infarction of the Posterior Portion of the Left Ventricle

ighthered are a present, not exaggerated

R-T₂ usually elevated, rarely isoelectric and never depressed

T, usually inverted

R-T; much elevated as a rule

T, usually inverted

Q_i frequently markedly prominent, Q pattern commonly present

O. usually within normal limits

T, usually inverted

to dilatation of the pulmonary vessels may be present (Fig 9)

Acute pulmonary embolism and acute coronary thrombosis may have the following symptoms in common sudden onset, pallor and sweating, precordial pain, weakness, vomiting, and collapse, marked fall in blood pressure, and acceleration of the pulse, leukocytosis, and elevation of temperature Marked cyanosis and urgent dyspnea are encountered much more frequently in cases of acute pulmonary embolism than in cases of coronary thrombosis. Pain is more severe and prolonged with acute coronary occlusion and usually is projected to the sternal region. The pain of pulmonary embolism usually is felt in the lateral regions of the thorax and may be made worse by inspiration. A previous history of angina pectoris should point to the possibility of coronary occlusion. In the accompanying table and in Fig. 10 are recorded the characteristics of the electrocardiogram in pulmonary embolism and in recent acute infarction of the posterior basal portion of the left ventricle with which pulmonary embolism is most likely to be confused

Mechanism of Death — Arguments against arterial obliteration and insuffi-

ciency of the pulmonary circulation being solely responsible for death are, as follows (1) In pulmonary surgery it is possible to ligate one or all the branches of the pulmonary artery on one side, (2) in some cases there has been time to remove the clot from the pulmonary artery by the Trendelenburg operation and (3) correlation between the size of the embolus and its fatal issue is lacking

Experimental studies on rabbits by M Villaret, L. Justin-Besangon and P. Bardin (1936) have shown that sudden death from pulmonary embolism may be due to reflex sympathetic inhibition, and that the susceptibility to sudden death may be increased by acidity and diminished by alkalinity. It seems quite possible that reflex spasm of the pulmonary arteries at the hilus may play an important role.

Prevention and Treatment Improvement in the rate of circulation and particularly acceleration of the return flow of blood from the lower extremities should be the aim in treatment On one surgical service at the Mayo Clinic the following postoperative program has been followed during the year just passed

'The patient is placed in the *Trendelen-burg position* for the first 24 hours after

operation Carbon dioxide is administered by inhalation several times in a day and night for the first 48 hours. Frequent deep breathing exercises are urged in every case. Attempts at early coughing are encouraged as much as possible. Extreme care is observed to keep the patient's legs warm at the operation, during his transfer to his room, and after his return to bed. Frequent massage of the legs is practiced during the first 48 hours and

Special postoperative treatment might well be limited to patients more than 40 years of age, unless obesity was present or there was suspicion of some circulatory defect. Also patients undergoing abdominal operations, particularly cases of malignant growth requiring a resection of a portion of a viscus, belong in this group

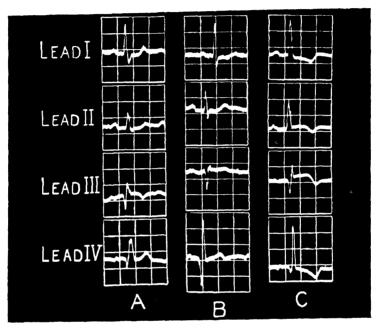


Fig. 10—Electrocardiograms in case 2. A, obtained October 5, B, obtained in the same case one veir later. (, obtained in a case of acute invocardial interction of the posterior basal portion of the lett ventricle. (Birnes. J. V. M. V. Oct. 23, 1937.)

twice daily thereafter until the patient is out of bed Passive and active movements of the extremities are insisted on at stated intervals from the time the patient is returned to his room and until he is out or bed. For purposes of control, thyroid extract has not been administered to these patients, although there is no reason why its administration should not be combined with this regimen. On this program no patient has died of pulmonary embolus following 750 consecutive operations, most of which were laparotomies, and while the series is too small from which to draw conclusions, the procedure will be continued and form the basis of a subsequent report"

Patients who have had a mild premonitory attack indicative of pulmonary embolism require greater care in regard to subsequent efforts on getting out of bed A syringe containing ½ gr (0.032 Gm) of papaverine hydrochloride for intravenous administration should be at hand. If Trendelenburg operation is to be considered, a sterilized surgical set should be available. An oxygen tent should be obtainable at a few moments' notice.

In the *treatment of an attack*, *papaverine* or other antispasmodic substances

should be given at once, with enough morphine to allay pain and combat the patient's anxiety. Patients should be placed in a semiupright position, being allowed to breathe air with a suitable concentration of oxygen. In case of marked venous distention and cyanosis, venesection may be indicated If the attack is survived, but with evidence of cardiac embarrassment, digitalis should be administered in suitable amounts. If the situation is desperate and a surgeon is at hand, the Trendelenburg operation should be considered

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VIII. HYPERTENSION

In General

In an article entitled "Thoughts on Hypertension," D Riesman¹ discusses the etiology, symptomatology and treatment of essential hypertension. Hypertension may be classified as follows

Classification

- I Primary essential or arteriolospastic
- 2 Arteriolitic or malignant
- 3 Nephritic
- 4 Secondary or accidental
 - (a) Aortic insufficiency
 - (b) Coarctation of the aorta
 - (c) Adrenal tumors
 - (d) Pituitary basophilism
 - (e) Hyperthyroidism
 - (t) Pregnancy
 - (ii) Enlarged prestate
 - the Arteriovenius aneurism

Subclasses

- 1 Juvenile
- 2 Superhypertension

Malignant hypertension is not believed to be a late stage of essential hypertension, in that it occurs earlier in lite than essential hypertension, the diastolic pressure is much higher than in the majority of cases of the latter renal changes are pronounced, the peripheral vessels are

thickened, tortuous, tense and hard, retinal changes are present, with pallor and sallowness, and cerebral accidents are common. In view of the necrotic inflammatory changes in the arterioles, the term arteriolitic hypertension is applicable.

By juvenile hypertension is meant a premature hypertension occurring usually from just before puberty to 35 years. This class includes cases in which the blood pressure has been repeatedly found elevated, 150 mm and upwards. Superhypertension is applied to cases in which the blood pressure is 260 higher. A considerable number of women with systolic pressures of 270 mm have been observed to live for many years.

Essential (Primary) Hypertension

This type is responsible for 15 per cent of all deaths after the age of 50 years, being the principal factor in what Riesman has termed the failing heart of middle life. The most striking objective result of essential hypertension is enlargement of the heart.

Etiology—None of the various theories advanced in explanation of essential hypertension has been proved. However, it is of interest that hypertension is uncommon among the Chinese. Even for eigners living in China tend to have lower blood pressures. This striking difference between the oriental and occidental has been attributed to differences in stature, muscular development, climate, habits of diet, but the greatest difference hes in their respective attitudes toward life. The placidity of the Chinaman is proverbial.

Psychologic Disturbances—Mental strain from business or domestic wornes, unsatisfied ambition disturbances in the sexual sphere, frustrations etc., seem to be capable of raising the vascular tonus. Heredity is an influential factor in hyper-

The variability, the labileness of the blood pressure in essential hypertension, the absence of structural (inflammatory or degenerative) changes in the arterioles in hypertensive individuals dying in the early stages, suggest that spastic constriction of the arterioles is the likely cause. The cause of the spasm is most probably chemical or hormonal in nature Perhaps at present too much prominence is being given to vasomotor mechanism and not enough to the intrinsic myogenic capacity of the blood vessels for constriction and dilatation IM Prinzmetal and C Wilson² have demonstrated in hypertension the presence of an intrinsic vascular hypertonus -on which normal vasomotor activity 15 superimposed —ED]

Symptomatology - Essential hypertension may be symptomless for many years, often being discovered accidentally during insurance or health examinations The mangural symptoms are mainly subteetive -dizziness, headache ringing in the cars, palpitation, slight dyspnea on effort a sense of weight in the chest, nose bleed and uritability Eventually such patients come under observation tor more pronounced symptoms, principally cardiac, cerebral or gastric cardiac manifestations are those of early congestive tailure-dyspinea, peripheral edema, basal pulmonary congestion or unilateral hydrothorax. A rarer symptom is acute pulmonary edema recurring at intervals, usually at night (See Treat-MINT OF LEIT VINIRICULAR PAILURE. p 393). An attack of angma pectoris or coronary occlusion may be either an carly or a late symptom. The electrocardiogram may show left axis deviation, in cases of long standing hypertension, there may be prolongation of the QRS interval beyond 0.1 sec due to increased conduction through a hypertrophied ventricle

Hemiplegia, aphasia, or monoplegia may be present due to local angiospastic states In severe cases generalized convulsions may occur, often being wrongly called urenuc or epileptic (which condition has been termed hypertensive encephalopathy, or epilepsia tarda) During the convulsive seizures, there is usually a sudden and abrupt rise in the systolic blood pressure, at times to 280 or even 300 mm The focal symptoms may last from a few minutes to 24 to 36 hours and may then subside without any vestige Hypertension may also lead to thrombus and to rupture of peripheral vessels (apoplexy), which is a frequent, but by no means the most frequent, mode of death in essential hypertension gastric symptoms, most commonly fullness and gaseous distention, are the result of myocardial weakness Such complaint by a person past 50 years, previously free of digestive disturbances, should never be considered lightly, in that it may indicate the beginning of malignant disease or the failing heart of long-tanding high blood pressure

Diagnosis—A systolic blood pressure of 140 to 150 mm in an individual under 40 years of age is not to be ignored. A family history of hypertension may be of significance. The criteria for the diagnosis of essential hypertension are

- 1 A persistently high systolic pressure
- 2 A relatively low diastolic pressure
- 3 Absence of disturbance of renal function
- 4 Normal blood chemistry, 1e, urea nitrogen and chlorides
- 5 Absent or minimal eye changes
- 6 Symptomatology trivial compared with the height of the systolic pressure

Prognosis—The following favorable facts may be useful in guiding the patient's mind

1 An individual can live to be 80 or even 100 years with high systolic blood pressure

- 2 Women bear high blood pressure better than men
- 3 The diastolic blood pressure is more important as a prognostic index than the systolic blood pressure. A low diastolic blood pressure tavors relative longevity.
- 4 Good renal function—traces only of albumin or no albumin, a few hyaline casts, good concentration—is a favorable prognostic finding
- 5 Moderate cardiac hypertrophy is not unfavorable
- 6 Cerebral accidents even of apparently trivial nature as well as anginal pain and retinal hemorrhages are all ominous signs

Treatment—The treatment of essential hypertension is in large part psychologic. Patients with essential hypertension must be assured of the comparative harmlessness of high blood pressure Many hypertensive patients overwork, overeat, undersleep and oversmoke, all of which departures from normal must be corrected. The man who takes to bed with him the "cares that infest the day" must be educated to a better habit. In regard to diet, quantity is more important than quality, especially if the individual is overweight. With the exception of those who include in meat and salt to excess, marked restriction, such as in the tormerly used salt-tree, low-protein diet is of no particular value in fact it may make the individual's life miserable little whiskey or a social glass of wine does no harm to the blood pressure However a minimal amount of smoking is advisable and if the patient has had cardiac pain, tobacco should be forbidden altogether. It necessary a laxative, such as mineral oil or compound licorice powder, should be prescribed Toxic symptoms—occipital headache and mental depression—are sometimes quickly relieved by colonic irrigation In particularly constituted individuals, a weekly dose of castor oil may prove

helpful Exposure to the hot sun should be avoided *Exercise* within reasonable limits is permissible. Wading in a swift stream to catch trout or salmon involves not only severe physical, but also an intense emotional strain, more than is good for a hypertensive fisherman. A prolonged golf game in the hot sun is likewise fraught with risk. Home gymnastics should be modified to suit the cardiovascular condition.

There is no specific drug that will permanently lower arterial blood pressure. The best results are obtained with sedatives, particularly the *barbituric acid* group *Phenobarbital* is very useful, the *bromides* are also helpful—a combination with elixir phenobarbital at times being of advantage *Chloral hydrate*, perfectly safe in reasonable doses, may also prove of benefit

When the pressure is high and the heart begins to labor or convulsions or acute pulmonary edema occur, venesection often brings immediate relief. In women at the menopause some of the endocrine products may be given trial, however, a great deal more is to be known before their being classified as sovereign remedies. When the pressure is abnormally high, the nitrites may be administered For regular use, erythrol tetranitrate in doses of 14 to 12 grain (0015 to 003 cm) is recommended In an emergency and when cardiac pain is present nitroglycerin under the tongue is the best remedy X-ray therapy has been used on the adrenals and on the pituitary gland, the latter on the theory that pituitary basophilism might be the cause of essential hypertension, however the data are as vet insufficient for a definite conclusion. Physiotherapy, including diathermy is of questionable

Surgical Treatment—\arious surgical procedures, consisting in the main of

cutting off the vasomotor supply to the abdominal arteries and arterioles, have been devised for the treatment of hypertension. One of the first attempts made to treat essential hypertension surgically was unilateral adrenalectomy, performed by Crile about 1910 Later partial resection of the other gland was added to the unilateral adrenalectomy, after which procedure the blood pressure was affected somewhat more than by the latter alone, but later it rose to the high level Denervating the glands in two stages, which was then tried, had a better effect, the improvement or cure lasting in some cases as long as five years, but recurrences were still The operation was then extended to include resection of the larger, minor and least splanchnic nerves, but even then results were less than anticipated so that another approach was chosen, vis, resection of the celiac ganglion and denervation of the aorta. The results of the latter in 25 instances, chiefly cases of malignant hypertension have been most encouraging

At the Mayo Clinic, two operative procedures have been employed (1) Extensive bilateral section of the ventral roots of the lower thoracic and upper lumbar nerves, (2) extensive subdiaphragmatic sympathectomy, which includes the splanchnic nerves on each side as well as the two upper lumbar ganglia and partial resection of the suprarenal glands. It is too early to draw definite conclusions as to the value of these operations, but from observations to date, the latter procedure is preferred ³

According to E V Allen and A W Adson,⁴ of the Mayo Clinic, the results of operation for essential hypertension can be predicted by observing the response of the blood pressure to rest and sleep, to sodium amytal administered by

mouth in doses of three grains (0 2 Gm) hourly for three successive hours, to administration of ½ grain (0 032 Gm) of sodium nitrite at half-hour intervals for three hours, and to the slow, intermittent, intravenous injection of a five per cent solution of pentothal sodium for light anesthetization. When poor results of operation were predicted by these tests, the outcome was almost uniformly unfavorable. Even when good results were predicted, some patients did not receive so much benefit from operation as was anticipated.

In a series of 85 cases, on whom bilateral subdiaphragmatic sympathectomy was performed, there were no operative deaths The operation does not disable, although anhidrosis of the lower extremities and loss of ejaculation and probably of fertility of the male may result Following operation, orthostatic hypotension and tachycardia occurred, but disappeared in time, the response of the blood pressure to immersion of the hand in ice water is Symptoms are relieved diminished when blood pressure is greatly reduced by the surgical procedure, and similar benefit may occur without great reduction of blood pressure. About 70 per cent of patients were improved clinically. As a result of operation, the heart may decrease in size, and inverted Twaves in the electrocardiagram may become upright, retinitis and spasm of the retinal arteries may diminish or disappear, albuminuria may decrease and renal function may be improved, and a decrease in basal metabolism may occur In 45 per cent of the cases the blood pressure was not materially reduced, but, many of these patients would not be selected for operation now in that preoperative tests would indicate that operation would not significantly reduce the blood pressure

about 30 per cent results in regard to blood pressure were fair, and in 25 per cent results were excellent.

In 17 patients at the New York Hospital, I H Page and G. J Heuer⁵ have performed section of the anterior nerve roots (usually of the ninth dorsal to the first lumbar nerve, inclusive), thereby abolishing the extrinsic vasomotor control of the splanchnic area Although the operation has markedly improved the clinical condition of many of the patients, followed for periods up to two and one-half years, its ultimate value in the treatment of hypertension has not been established

In their most recent article, in which the results of the splanchnic nerve resection are reported, I H Page and G J Heuer⁶ state that the operation was well borne in all patients without any complications or fatalities. The operation consisted in bilateral resection of segments of the great, small and, if present and found, the smallest splanchnic nerves together with the three lower dorsal gangha, the operative approach was above the diaphragm. There were six cases of essential hypertension (aged 25 and 48 years; varying in degree from mild to severe one (aged 25 years) with early malignant hypertension, and two (aged 18 and 25 years) with severe malignant hypertension The reduction in arterial pressure following operation was marked within six months it had returned to the preoperative level in all patients Subjective improvement - consisting of lessening in frequency and severity of headaches, case of fatigue nervousness, tenseness and irritability - occurred in the six patients with essential hypertension, but in three instances improvement lasted less than a year. Improvement in the cases of malignant hypertension was transient

Renal efficiency was unaffected by the operation. Also, judging by electrocardiographic records and x-ray examinations, there was apparently no marked effect on the heart. No consistent change was observed in the pressor response to immersion of the hands in cold water. In one case of essential hypertension and two cases of malignant hypertension papilledema disappeared, but within several months reappeared in the latter cases Reduction in intensity of the constriction in the retinal arterioles occurred in all cases with the exception of one with malignant hypertension, demonstrating that arteriolar relaxation occurin regions other than those denervated, in most of the patients constriction returned after several months by the authors, the therapeutic results in this small, but representative, group of cases do not appear encouraging

Class Method in Treatment—Class instruction in the treatment of essential hypertension, practised in the Medical Clinic at the Boston Dispensary, is discussed by R. W. Buck? The aim of the clinic is to present to patients a program of living which will enable them to live consistently at the optimal level of well-being. Attendance of patients with advanced renal failure is not encouraged.

As demonstrated by D. Ayman Suggestion is an important factor in the treatment of essential hypertension. Suggestion, by inspiring confidence as to the benefits of treatment relieves worry quiets the patient—thereby accomplishing relaxation probably as effective as that obtained with luminal, alcohol, the mitrites, waterinelon seed extract inistletoe, or surgery of the sympathetic nervous system. When a patient joins a group his individuality merges with it,

and his individual resistance to suggestion is overcome by the contagion of the group response to its leader. Class instruction encourages competitive striving for results, it causes the members to try to emulate those who are most successful, it develops a spirit of cooperation and enthusiasm which is possible only in a group with a common objective.



lig 11—The Rule of the Class (Buck Ann Int Med Sept 1937)

The program is built about a threefold approach illustrated graphically by a triangle, each side of which represents one aspect of the treatment (Fig. 11) Medical care includes such matters as the treatment of varieose veins, diabetes, smusitis or congestive heart failure Diet is a rather arbitrary attain diet is that which Hindhede promulgated in the Scandinavian countries for many consisting simply of potatoes baked and caten with the skins intact dark bread and butter, milk, and apples or other tresh truit. This diet may be varied by occasional mild lapses on holidays or special dinners. Suggestion and psychotherapy, in the form of education and explanation, form the real basis of the method The relatively benign course of essential hypertension is stressed, a plausible theory of its pathological physiology is presented, and the

importance of physical and nervous strain in the development of symptoms is emphasized. The important rôle of the emotions, apprehension, worry and unpleasant thoughts in the genesis of symptoms is pointed out repeatedly.

At each class meeting the importance of regular and systematic relaxation is stressed. There is a 5-minute relaxation period at each meeting during which all individuals in the room are asked to follow the demonstration by the leader The effect attained by the proper conduct of this 5-minute period of complete silence and repose is quite marked. The class members practice their "relaxation exercise" once, twice or three times daily during the week. The giving of "testimony" by the older members is a powerful factor in starting the new members off in the proper spirit of optimism and earnest attention to the rules The "progressive relaxation" of Jacobsen (1934) has not been practised in that the method is too time-consuming—calling for too much individual attention

The results over a period of several months have justified expectations. The uniformity with which patients report teeling fine, when formerly a variety of symptoms was present, testifies to a new mental attitude, if not to any modification of the underlying pathological process. Some patients have shown no striking change in the blood pressure level, but in two-thirds of those who have made three or four visits to the class, a fall in pressure of from 18 to 46 mm of mercury has been observed. A worthwhile result has been accomplished it the patients lose their fears, adapt themselves to their condition, and become optimists rather than pessimists

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IX. CARDIAC NEUROSIS

As stated by P D White and R E Glendy, 1 every patient with cardiac symptoms or signs or with knowledge of heart disease in family or friends is a potential cardiac neurotic Cardiac neurosis consists essentially of fear or apprehension about the heart, which may prove very severe and crippling Early recognition and treatment is essential, in that a long established neurosis may be almost incurable

Some very definite exciting factor is present in every case. The occurrence of heart disease, especially of heart deaths among family or triends, may initiate a cardiae neurosis in an individual who is ready for a neurosis of some sort. The finding of a heart murmur (trivial or not) or some disturbance of rhythm which may be insignificant, of hypertension (great or slight) or of actual heart disease may be the Subjective sensaprecipitating factor tions such as extrasystoles a paroxysm of tachycardia, the manifold symptoms of neurocirculatory asthema, sighing respiration, true dyspnea, angina pectoris the prolonged pain of coronary thrombosis, and the various pains in the center or lett side of the chest of noncardiac origin (due to cardiospasin, bursitis and pleurisy strain, muscle may be the starting point The most difficult cases are those with serious heart disease complicated by car-

diac neurosis. It is a common experience that nervous prostration or a severe cardiac psychoneurosis following coronary thrombosis, especially in physicians, is more difficult to treat than the myocardial infarction itself.

Five striking examples of cardiac neurosis are presented by the authors.

Case I—A young unmarried male teacher, aged 37 years, had as a basis a hypersensitive nervous system, a history of heart disease in the family, access to medical literature, increased nervous tension in his work, and a hasty, incorrect diagnosis of angina pectoris, also excessive use of tobacco may have been an aggravating factor

Case 11—A female, aged 46 years, whose first heart attack apparently consisted of paroxysmal tachycardia with precordial distress following the death of her only child, was unfortunately treated with morphine. During the next 15 years she became a morphine addict, and never showed any evidence of heart disease.

Case III-A soldier, aged 29 years. whose rheumatic heart disease was discovered while suffering from neurocirculatory asthenia following influenza, and for which he was discharged as partially An exacerbadisabled from the army tion of symptoms followed some years later when his pension was discontinued and became so severe that it was contused with angina pectoris and treated with morphine and paravertebral alcohol injections of the upper left dorsal sympathetic ganglia. In spite of the resulting anesthesia over the left chest and vasodilation of the left arm and hand (indicating a sympathetic block), the attacks of pain continued as before until it became evident that he did not have angma pectoris

Case $II = \lambda$ physician and naturalist, aged 58 years illustrates the mental

depression and neurotic apprehension which often follows coronary thrombosis, and which might be overcome through reassurance and the readjustment of activities and interests

Case I'-A manufacturer, aged 34 years, presented a history of serious heart disease consisting of coronary thrombosis, masked by psychoneurosis and morphinism, with the electrocardiograms giving the necessary clues to the correct diagnosis, but, coronary disease was in a large part overlooked or minimized because of his youth, obvious nervousness, addiction to morphine, and relatively normal physical examina-Diagnostic paravertebral novocame injection of the upper dorsal sympathetic ganglia afforded almost complete relief from pain during a severe episode, which fact so impressed him that he wished to have a resection of the sympathetic nerves regardless of the risk. The latter was attempted but he did not survive (illustrating the hazard of radical neurosurgery in contrast to nerve injections in the presence of severe coronary disease) This case reveals the danger which might attend enthusiasm in the diagnosis of cardiac neurosis with failure to recognize the presence of serious heart disease which might lead to early death

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X CARDIOVASCULAR DIS-TURBANCES DUE TO NUTRI-TIONAL DEFICIENCY

Nutritional factors which may be responsible for cardiovascular disturbances have been called to attention by S Weiss and R W Wilkins ¹ Both deficiencies and excesses of food may lead to disturbances of the circulation. The

clinical manifestations of certain vitamin deficiencies are conditioned not only by the total caloric intake and the total amount of energy expended, but also by the proportional intake of carbohydrate, protein and fat Disorders of the gastrointestinal tract causing alterations in motor and secretory functions and in absorptive capacity may so interfere with the utilization of dietary factors that deficiencies may develop in the body in spite of an adequate supply by mouth Damage to the liver impairs the metabolism of vitamin A and protein, and also may be responsible for other deficiency syndromes Judging from the behavior of vitamins B and C, symptoms are liable to develop when with a deficiency of vitamins there is present simultaneously an elevated metabolism (caloric vitamin ratio of Cowgill), which latter may result from increased muscular activity, increased caloric intake, fever, hyperthyroidism and the Under such conditions, specific metabolic processes influenced by or dependent on vitamins may become disturbed, and harmful products may accumulate, — a fact well-illustrated chronic alcoholic patients when suffering pneumonia or typhoid fever times, patients with mild manifestations of avitaminosis show temporary aggravation of symptoms when given a diet rich in vitamins and calories

Among the *nutritional excesses*, increased intake of calories as manifested by obesity frequently exerts harmful effect on the heart and particularly on the circulation. There is no substantial evidence indicating that a diet disproportionately rich in vegetable or animal protein causes cardiac or vascular disease. Feeding of cholesterol to certain species of animals can induce atherosclerosis ("cholesterinsteatosis") and through it heart disease, but the significance of

cholesterol of the diet in the causation of human arteriosclerosis is not established. In diabetes a high fat diet appears to be apt to cause arteriosclerosis. Excesses of water and of mineral constituents play no appreciable role in circulatory disturbances, except through indiscriminate use in postoperative states and in patients with heart disease. There is no conclusive evidence that hypervitaminosis plays a rôle in the causation of functional or structural changes in the human cardiovascular system The arteriosclerosis produced in animals with large doses of vitamin D has nothing in common with human arteriosclerosis The rare instances of cardiac damage attributed to vitamin D cannot be accepted as due to hypervitaminosis

Caloric Intake (Undernutrition and Inanition)—Fasting or severe restriction of diet results in a bradycardia of from 30 to 40 per minute, a decrease of the arterial pressure, and a lowering of the metabolic rate. Since the blood flow is related to the level of the oxygen consumption undernutrition is presumably associated also with decreased blood flow and cardiac work These circulatory changes, if maintained for a short period, may exert a beneficial effect in congestive heart failure caused by organic heart disease, as demonstrated by S. H. Proger and H. Magendantz 2 Prolonged undernutrition, on the other hand causes changes in the myocardium with intracellular deposition of fat (fatty degeneration) and decrease of interstitial fat animals and man, chronic malnutrition results in considerable loss (from 20 to 30 per cent) in cardiac weight, while in malnourished young animals and children the loss is slight. In general the degree of loss in heart weight is somewhat less than that in total body weight. The association of famines with

epidemics of infectious diseases suggests a lowered resistance of these patients, especially to infections. Evidence is lacking, however, to indicate that chronic undernutrition is responsible for vascular disease.

Proteins—The rôle of proteins in the maintenance of the osmotic pressure of the circulating blood is well established Chronic protein deficiency leads to edema, which may be generalized ("nutritional edema")-exerting a harmful effect on the circulation, particularly when involving the lungs In chronic heart disease, a low protein content of the blood associated with high venous and hence high capillary pressure may give rise to pleural and peritoneal transudation, and may increase the tendency to cardiac asthma and pulmonary edema In conditions associated with continuous protein loss, such as occurs in pleural or peritoneal exudates and transudates requiring repeated taps, particular effort should be made to reestablish the normal protein content of the blood by means of adequate protein in the diet

Carbohydrates—Reduction in the blood sugar below a certain level results in syncope, circulatory collapse and convulsions—with a fall in the arterial pressure. Such states occur as a result of hyperinsulmism, caused either by overdosage or by abnormal production as in certain hyperplasias and tumors of the islands of Langerhans and other glands of internal secretion.

Water and Salts—Dehydration and salt depletion occur relatively frequently, constituting grave danger to the organism mainly through circulatory collapse and shock Whether water restriction can reduce the cardiac weight, and thereby produce circulatory failure is not definitely established, although there are reports indicating that animals dying from thirst can lose from 30 to 40 per

cent or more of their cardiac weight Normally between 750 and 10,000 cc of fluid is secreted into the intestinal canal within 24 hours. In health the greater part of this fluid is reabsorbed, while in certain pathologic conditions, particularly those associated with vonuting and diarrhea, most of it together with its organic and inorganic constituents, may be lost, rapidly leading to reduction of blood volume with hemoconcentration and with accumulation of toxic waste products, and, finally to fatal collapse and shock 3 In diseases associated with fever, fistulous opening (as in biliary and pleural fistulas), heat exhaustion, adrenal insufficiency, or vomiting with pyloric stenosis, the adequate replacement and supply of water and salts are most effective measures in the prevention of peripheral tailure of the circulation Collapse and shock of dehydration and of "hypochloremia" may also result from the indiscriminate use of gastric or duodenal drainage with suction ('Wangensteen tube") such as in vogue at present in certain surgical and medical conditions, which often are already associated with a tendency to collapse and shock. The relative rôle of low blood chlorides in the circulatory collapse associated with vomiting and alkalosis is not clearly understood as yet

Iron and Certain Other Nutritional "Extrinsic" Factors — Deficiency of non and of certain protein derivatives essential for normal blood formation produces—through hypochronic and macrocytic anemia—changes in the circulation, characterized mainly by an increase in the velocity of blood flow and cardiac output, by fall in the arterial pressure and frequently by an increase in pulse pressure. While by x-ray examination the cardiac shadow is increased in but eight or nine per cent of the cases with a hemoglobin content of from

56 to 65 per cent, it is increased in all cases with a hemoglobin level as low as 12 to 15 per cent. In pernicicus anemia fatty degeneration of the myocardium, accentuated around the venous ends of the capillaries, can occasion the "tiger hily" appearance of the cut section. The cause of cardiac enlargement in some cases of anemia remains obscure since it cannot always be related either to increased work of the heart or to the degree of anemia.

Systolic murmurs over the apex and base of the heart are frequent in anemia as a result of dilatation of the heart Rarely, in severe anemia, transient diastolic murmurs occur, which with improvement disappear long before the subsidence of systolic murmurs Patients with severe anemia often suffer from palpitation, also there may be a tendency to syncope Rarely anemia may precipitate congestive failure, as well as angina pectoris, even without coronary disease In pernicious anemia, angina pectoris may occur during treatment, presumably the result of a sudden increase of cardiac work without simultaneous increase of cardiac strength

Vitamins—Deficiency of vitamin B_1 is related to beriberi, and of vitamin B_2 to pellagra. In the United States these diseases frequently occur in the same patient in a combined form

Beriberi—The most important of the vitamins in relation to the heart is B₁. For centuries beriberi has been known as a devastating disease of the rice-eating peoples of the Orient. Subsequently it was found to occur in South America, Africa, Labrador, and the United States. In the Orient the disease has been known in the "dry" form which manifests itself mainly in the muscle wasting and peripheral neuritis, and the "wet" form which is associated with cardiovascular disturbances, and generalized edema

Strenuous exertion is a dangerous aggravating factor in beriberi, and severe neuritis, by making work impossible, may protect against serious or fatal circulatory failure. In the acute "permicious" type, death of cardiac origin may occur with unexpected rapidity. The cardiovascular disturbances of beriberi of the Orient have been described by J. Shimazono (1931) and by K. F. Wenckebach (1934). Psychic, gastrointestinal, inictabolic, henuc, and bony disturbances are often present.

The discovery of beriberi as a disease of regular occurrence in the United States arose through recognition of the tact that certain types of neuritis are related to nutritional disturbances, particularly lack of vitamin B. This observation suggested the possibility that if certain types of polyneuritis are caused by deficiency of vitamin B, some of the patients should present cardiovascular manifestations, such as in beriberi of the Orient. In an analysis of some 900 cases of nutritional deficiency, including general malnutrition, chronic alcoholism with or without polyneuritis, pellagra, neuritis of pregnancy and diabetes. Weiss and Wilkins4 found 85 cases in which cardioxascular dystunction could not be ascribed to the usual etiological factors In addition, they studied 35 cases from 5506 medical admissions to the Boston City Hospital within a period of two years. However the disease is far more common than is indicated by the frequency of the cardiovascular manitestations, since in the majority of instances it is manifested in neurologic Most of the patients disturbances only drank large amounts of alcohol regularly, in a smaller group drug addiction, pregnancy, diabetes, gastrointestinal disease, psychic peculiarities (food fads). and poverty played a role. The patients were usually well nourished, with caloric intake adequate or more than adequate, but with an estimated vitamin B (B_1) intake less than that indicated by Cowgill as hable to produce polyneuritis. Many of the patients also had symptoms of pellagra, and a few had scurvy

The most common cardiovascular symptoms of beriberi are dyspnea on exertion, associated with palpitation, tachycardia and embryocardia Gallop rhythm, prominent cardiac and epigastic pulsations and bounding peripheral pulses with sounds ("pistol shots") are frequently present. The heart may be normal in size or enlarged, and systolic and rarely diastolic murmurs may be heard Cardiac asthma (paroxismal dyspnea) has also been observed. Signs of pulmonary congestion are frequently present, and cloudiness of the lung fields is seen on x-ray examination. The arterial pressure is usually normal, with a tendency to increased pulse pressure, in some cases the systolic pressure is moderately elevated during the acute stage of circulatory failure, but it returns to normal when the patient's condition improves. The veins of the neck are normal or engorged, as confirmed by the normal or elevated venous pressure The skin is usually warm and of normal color at times evanosis is present Edema, either dependent or diffuse, is tremently present. Patients with severe cardiovascular manifestations are prone to develop tever, which in turn, aggravates enculatory failure. Sudden circulatory collapse without premonitory symptoms occurred in a few patients

In 67 cases presenting normal blood pressure and no clinical evidence or organic heart disease, the electrocardiograms disclosed abnormalities in all but five instances—the most common finding being alteration in the T-waves and prolongation of electrical systole (Q-T). The hemodynamics were characterized

by low vital capacity of the lungs, high venous pressure, and normal arterial pressure, and by relatively or absolutely increased velocity of blood flow with decreased peripheral utilization of arterial oxygen. The osmotic pressure of the blood usually was moderately low There was often an increase in the bisulfite binding substances in the blood In the majority of instances postmortem examination reveal the weight of the heart to be normal and a moderate dilatation of the right ventricle. In only 9 out of 30 cases was there an increase in weight and a considerable degree of dilatation of the cardiac chambers, particularly the right ventricle The histologic changes, hydropic degeneration of the myocardial fibers. swollen collagen, perivascular "edema" and separation of the myocardial bundles were identical with those described by Wenckebach

of Beriberi Cardiovas-Diagnosis cular Disease-This is facilitated by the frequently simultaneous presence of certain noncirculatory manifestations of dietary deficiency, such as peripheral neuritis, psychosis, glossitis, diarrhea, dermatitis, anemia, hypoproteinemia, dvsphagia, hoarseness, dry and irritating cough, aphonia and purpura. In differential diagnosis, the absence of recogmized etiologic causes of organic heart disease and the history of an abnormal diet or intestinal dysfunction may be helpful. The combined presence of congestive failure of the circulation and a relatively or absolutely increased rate of the circulation is the most outstanding characteristic of the condition Assured diagnosis may depend on complete recovery after rest and vitamin B therapy

It is of interest that the infantile type of beriberi in Japan and the Philippines occurs mainly among breast fed rather than among artificially fed babies, which

suggests that beriberi and avitaminosis of the mother may have an important bearing on the nutritional state not only of the new-born, but also of the nursing infant Whether some instances of "idiopathic" cardiac hypertrophy might be explained on this basis is not known at present (The subject of the child's heart in avitaminosis has recently been reviewed by I A Abt.⁵)

Treatment of Beriberi-Some patients show improvement on a deficient diet when simply put to bed, others may show sudden aggravation of symptoms or even fatal collapse when kept in bed and on a deficient or even a normal diet Digitalis and diuretics are of benefit in some instances Diets rich 111 vitamins (particularly $B(B_1)$), extracts rich in B₁, and crystalline B₁ are beneficial Some patients improve rapidly, and the clinical course may show a dramatic change within a week, with a loss of 30 or 40 pounds (136 or 181 ke i of edema fluid, in others the improvement is slower, recovery requiring from four to six weeks. In general, improvement is most rapid in patients with a severe degree of congestive failure of relatively short duration

Following the intravenous administration of from 5 to 10 mg of crystalline vitamin B_1 , three or four times daily, to patients kept during a control period on a deficient diet, the first change observed was the increased peripheral utilization of oxygen and slowing of the blood flow as a result of the disappearance of the arteriolar dilatation, occurring as early as 24 hours after the first dose Simultaneously there were symptomatic improvement and often marked diuresis, followed by a slow rise in the vital capacity of the lungs and a decrease in cardiac size. The changes in the electrocardiogram were the last to disappear, which fact is in contrast with the situation in animals deficient in vitamin B₁, in which the changes in the heart rate and in the electrocardiographic complexes may be abolished as early as four to six hours after subcutaneous administration of five micrograms of crystalline B₁. Administration of parenteral doses as large as from 30 to 100 mg daily for five to eight days, followed by oral administration of large amounts of B₁ extract, did not cause any detectable changes in the cardiovascular function of normal subjects or of nondeficient patients with organic heart disease or with various types of edema Improvement was usually more rapid and complete in the cardiovascular than in the neurologic disturbances, the only exception being the occasional rapid disappearance of psychosis after the administration of large amounts of vitamin B₁ In view of the frequent presence of multiple deficiencies in beriberi, attention should be paid also to the correction of the anemia with iron and liver extract, of the hypoproteinemia with a high protein diet, and of the hemorrhagic tendency with cevitamic acid

H Hashimoto" reports a case of acute permetous beriberi-a Japanese boy. aged 15 years, an apprentice to a plasterer, complaining of excessive fatigue, paresthesia of the legs, edema, vomiting, severe palpitation, dyspnea, and precordial distress even at rest-showing inverted T-waves in Lead I, who under intravenous administration of purified vitamin B1 recovered within about 50 hours from the acute cardiac failure-the electrocardiogram returning to normal Before treatment x-ray showed cardiac enlargement to the right and to the left The vitamin extract was given in the form of 1 cc of oryzanin fortior decemplex, Sankvo, once or twice daily, -each cc of the clear solution containmg 0.5 mg of purified crystals of vitamin B₁, corresponding in efficacy to 200 Gm of fresh rice bran.

Rôle of Alcohol in Beriberi-Alcohol is a food substance par excellence in its capacity to supply the body with necessary calories but with a minimum of vitamin B, which is an ideal combination for beriberi, since high caloric and low vitamin B₁ intake rather than general manition precipitates the clinical vitamin deficiency. The gastrointestinal changes often present in chronic alcoholism may well interfere with the absorption or utilization of the available vitamin B₁, while alcohol itself, a freely diffusible substance, is absorbed readily It is known that if B₁ avitaminotic animals are kept on a diet that is rich in fatty acids instead of carbohydrates, the manifestations of B₁ deficiency may be prevented. Polyneuritis, pellagroid lesions, and cardiovascular dysfunctions disappear on continuous alcohol intake provided vitamin B is administered simultaneously

The origin of the "beer heart" cannot be explained on the basis of increased intake of alcoholic fluids. It is probable that such instances of cardiac hypertrophy represent unrecognized cases of hypertensive heart disease, also, it has been suggested that beer drinking causes nephritis with subsequent cardiac hypertrophy.

Pellagra — Patients suffering from pellagra may exhibit cardiovascular symptoms which are attributed to the frequent association of the vitanim B₁ component in the deficiency. There is no experimental evidence that lack of vitanim B₂ is responsible for cardiovascular disease.

Vitamin C—The relation of deficiency of vitamin C to capillary fragility is established, but its role in cardiac disorders is not well understood Fxperimental scurvy in animals has been

observed to cause hemorrhages into and fatty degeneration of the cardiac muscle J F Rinehart⁷ has stated that scorbutic guinea-pigs respond to superimposed infection of beta hemolytic streptococci with degenerative and proliferative changes in the heart valves and myocardium—which observation has not been uniformly confirmed

In a study of the effect of acute scurvy on the gumea-pig heart, J McBroom, D A Sunderland, J R Mote, and T D Jones' found degenerative changes in the cardiac valves and myocardium, as well as definite proliferative lesions along the line of closure of the valves These lesions were equally prevalent and severe in total scurvy, whether or not there was superimposed infection, which fact difters from the findings of J F Rineheart and S. R. Mettier⁹ who reported striking differences in the frequency and severity of the lesions as between infected and non-infected scorbutic animals is possible that the diet used by the latter investigators was capable of producing only moderately severe seuryy and required added intection to produce total scurvy. The complete pathologic changes of theumatic fever are dissimilar from those of senity even though in some of the microscopic lesions of the valves there are certain points in common, 712 a subendothelial proliferative reaction with a cellular infiltration and a collagen Although scurvy may indirectly be a factor in lowering the general resistance of the body to infection, there is as yet no evidence that rheumatic fever and scurvy are the same disease, or that there is a direct causal relationship between them, even with infection by the hemolytic streptococcus complicating the latter. The lesions in the guinea-pig heart described by Rinehart and Mettier may be produced by acute scurvy alone, and may be interpreted as an attempt at repair of lesions caused by physiologic stress on a tissue weakened by acute scorbutus

S. Taylor¹⁰ also states that scurvy alone produces cardiac lesions in the guinea-pig and that added infections increase neither the incidence nor the Experimental severity of the lesions "scorbutic carditis" if allowed to become chronic results in congestive failure In such hearts the lesions cannot be cured with the administration of cevitamic acid Vitamin C, therefore, can prevent such lesions, but cannot cure them pathologic changes in scorbutic carditis, described by Taylor, are those of nonspecific valvulitis, myocarditis, and occasionally pericarditis. The lesions often contain gram-positive organisms, even though no organisms were injected In the acute lesions neutrophilic leucocytes predominate, while in the chronic lesions endothelial cells, lymphocytes, and fibroblasts are more abundant Giant cells and vegetations are not present

Changes in the myocardium have been described in human scurvy, but it is questionable whether they can be attributed to vitamin C deficiency. During the last few years the relation of vitamin C deficiency to theumatic fever and theumatic heart disease has been extensively investigated. The studies indicate that in rheumatic fever, as in other chronic infections, due to inadequate intake and/or to increased utilization of vitamin C, the cevitamic acid of the blood is low and the body 18 partially depleted of its normal storage The capillary fragility of some of these patients is often increased and can be reduced by the administration of cevitamic acid, on the other hand, vitamin C fails to influence the clinical course or reduce the incidence of recurrent attacks of rheumatic manifestations, -therefore, a causative relationship between vitamin C deficiency and rheumatic fever does not exist. However, in spite of these negative correlations, it seems advisable to feed rheumatic patients with a balanced diet rich in vitamins, including vitamin C.

The increased vascular fragility in vitamin C deficiency may lead to extensive hemorrhages and tissue damage. Not infrequently the level of the cevitamic acid in the blood of chronic alcoholic patients is low, and the consequent tendency to vascular fragility may contribute to the occurrence of epidural, subdural and intracerebral hemorrhages so frequently observed after relatively slight or no trauma in such patients.

Vitamin D—Cardiac changes with right ventricular hypertrophy in rickets occasionally have been observed. However, at present the assumption is justified that these changes may be attributed to the simultaneous presence of vitamin B₁ deficiency.

Conclusion—It is important to keep in mind that vitamin deficiency is followed by changes in the intermediary metabolism which cause (1) "biochemical lesions", later (2) functional and, finally (3) structural lesions. The principles of "deficiency" and toxicity" are interdependent, and not mutually exclusive

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XI. PERICARDITIS

In a discussion of pericarditis, A M Shipley calls attention to the fact that in coronary thrombosis pericarditis with e fusion may be confined to the area of myocardial infarction. The amount of effusion is usually small, however, occasionally considerable fluid is present and may cause uncertainty as to diagnosis, especially if coronary thrombosis occurs during the course of some infectious process, such as pneumonia, furunculosis, osteomyelitis, or peripheral infections during the course of uncontrolled diabetes.

For dramage of early cases of suppurative pericarditis a choice of anterior operations may be made trans-sternal, right or left parasternal, chondroxiphoid. or a combination of the sternal or left parasternal,—all of which should be as low as possible. In late cases with a large effusion, anterior drainage may not be effective and a posterolateral approach (as far as the pericardium is concerned) may be made by resection of the seventh rib near the midaxillary line. In all cases of this procedure reported, the pericardium was adherent to the pleura and pericardiotomy was possible without producing pyopneumothorax

ramponade of the heart is associated with pericarditis with effusion (whether purulent or scrous), with constricting pericarditis, and with compression due to other causes. Tumor of the heart and pericardium while rare, may cause serious compression of the heart, either because of the presence of the tumor itself or because of the effusion. Pneumopericardium may cause compression, and mediastinal tumor and ancurysm may be extrapericardial causes of tamponade. After compression of the chest with injury to the heart there may be early or late hemorrhage into the pericardial sac.

Tamponade is most dramatic in hemopericardium, especially if there is a penetrating wound into one of the cavities of the heart. In suppurative pericarditis the symptoms of tamponade may be secondary in importance to those of infection, and in slowly forming serous effusion large quantities of fluid may be present in the pericardium with no outstanding symptoms of compression of the heart. In rapid bleeding the heart is seriously embarrassed when from 200 to 250 cc. is present, while in slowly forming serous effusion, one to two liters of fluid or more may be present.

In acute tamponade, diagnosis must be made quickly, while with chronic tamponade every diagnostic aid may be used The outstanding symptoms of tamponade are high venous and low arterial pressure, with a paradoxic pulse and suppressed heart sounds. If the tamponade is acute and developing rapidly, anoxemia of the central nervous system, going on to unconsciousness occurs, if chronic, there will be congestion and enlargement of the liver with ascites and anasarca Physical signs consist of an enlarged cardiac-pericardial shadow with the base of the triangle caudate, and x-ray examination shows this enlargement and alteration in shadow, as well as a relative absence of pulsations along the margins of the shadow made by the shadow of the heart and the right diaphragm is also absent. When the fluid is free, most of it lies dorsal and lateral to the heart, and the apex is usually close up against the anterior layer of pericardium. Heart sounds are muffled not because the heart is pushed away from the listening ear, but because compression interferes with their quality

Chronic Adhesive Pericarditis

This may be divided into four types anatomically

- 1 Adhesions may be present between the two layers of the pericardium without constriction and without fixation of teh outer layer. Usually such adhesions are not productive of cardiac disability, and may be of value to the heart in establishing a new vascular bed in cases of coronary occlusion. Adhesions of this type may follow drainage of the pericardial sac for pyopericardium, and the heart function may be very little disturbed.
- 2 Another type of pericardial adhesion without serious cardiac disturbance is seen in pulmonary tuberculosis with adhesive pleuritis, the adhesions fastening the pleura or diaphragm to the outer layer of the pericardium. Such adhesions may be responsible for displacement of the heart in fibroid phthisis
- 3 Chronic constrictive pericarditis has become established as a separate and distinct entity, being recognized as a disease calling for surgical treatment. There is confusion as to a possible relationship to rheumatic fever and tuberculosis There are a number of reports of tubercles in acute and subacute cases, but in the chronic cases, although fibrosis is constant and calcareous deposition in the pericardium often present, tubercles According to E H are rarely seen Cushing and H S Feil² microscopic examination of the resected pericardium of 11 cases of adhesive mediastinopericarditis showed "the parietal and visceral lavers to be fused and indistinguishable with densely fibrous and hyalinized tissue, which was poorly vascularized Occasionally small collections of lymphocytes were observed Some of the cases showed focal areas of calcification There were no changes that could be construed as characteristic of rheumatic or tuberculous infection"

As stated by E D Churchill,³ active tuberculosis of the pericardium may produce the entire syndrome of chronic

constrictive pericarditis. "The probability that many of the cases of chronic constrictive pericarditis represent healed stages of pericarditis due primarily to tuberculosis is an important question still to be settled. Examination of the scar tissue removed at operation universally fails to establish a diagnosis of tuberculosis. On the other hand, the frequency with which calcium deposits are found, and the unusual density of the scar tissue tend to link the pathology with the tubercle bacillus. The only reliable finding that distinguishes the active phase of tuberculous pericarditis from constrictive pericarditis due to a healed scar is the demonstration of the tubercle bacıllus in fluid aspirated from the pericardium. The sudden appearance of the syndrome in a patient with known active tuberculosis elsewhere is presumptive evidence"

The incidence of tuberculous pericarditis varies from 07 to 11 per cent in different reports from autopsy records. Probably tuberculous pericarditis will in time be classified in three groups. (a) acute in which effusion predominates (b) subacute, in which adhesions and thickening are outstanding, and (c) chronic, in which fibrosis and constrict on are present. There is little evidence that previous drainage of the pericardial sac causes constrictive pericarditis.

Churchill advises against operating upon individuals with acute tuberculous pericarditis, even when symptoms of compression are present, in that repeated aspiration may offer some hope of survival until the chronic stage is reached when pericardiectomy may be done. During the active infection the effects of tamponade can be somewhat controlled by repeated aspirations and diuretics. Rest, light treatment, and other general measures may be employed as in tuberculous peritonitis. The value of pneumo-

pericardium or the possibility of oleopericardium under these conditions have not as yet been established

A triad of symptoms present in constrictive pericarditis, emphasized by (S. Beck, are (a) high venous pressure and low arterial pressure, (b) enlarged liver with ascites, and (c) a small quiet heart.

Treatment of Chronic Surgical Constrictive Pericarditis - Schmeiden (1926) practised an intercostal incision in order to reach the left side of the heart, while others have done some variation of the Duval-Barasty (1918) procedure (median sternotomy) Recently a third approach has been used, a long curved incision through the soft parts extending from the second to the sixth rib, running roughly parallel with the left margin of the sternum. After the flap of soft tissue is turned out, the ribs, cartilages, periosteum, and left margin of the sternum are removed By this procedure is exposed a large area of the anterior layer of the pericardium, sufficient for performing a wide decortication of the heart. Considerable difference of opinion exists as to the effect of atmospheric pressure on the exposed heart and great vessels, but, no surgeons disregard this factor, taking care to have at hand the means of differential pressure anesthesia in order to control collapse of the lung, if the pleura is opened, which usually happens. The wound should be closed snugly, layer by layer, and made airtight, every precaution being taken against infection. Dramage should be avoided if possible

4 In mediastinopericarditis heart, pericardium, chest wall, and diaphragin are all bound together, and during systole the heart contracts against a pull that is unyielding as far as the wall of the chest is concerned, and both the heart and the diaphragin are hampered

in their movements. The symptoms vary, depending upon the extent and denseness of the adhesions and on the time factor If the function of the heart is disturbed, myocardial changes gradually take place and the heart may become enlarged and finally undergo degeneration hesive nature of the malady may be evident in retraction of intercostal spaces during systole. The operative treatment is the cardiolysis of Brauer which consists of removing enough of the bony wall of the chest over the heart to liberate the heart and lessen the tug on the diaphragm, the mediastinal tissues and the lungs. It is an extrapericardial operation throughout. In most instances it is confined to resection of the cartilage and anterior ends of the left fourth, fifth and sixth ribs, together with a portion of the sternum. The patient may be a bad risk and the choice of anesthesia difficult Postoperative complications are dangerous, and great care should be taken in the diagnosis, preparation of the patient, and after care. Myocardial changes with hypertrophy, occurring in patients with this condition—also presenting a history of rheumatic fever are probably caused by the rheumatic tever, valvular disease, or hypertension rather than by mediasimoperical ditis

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XII. SIZE OF HEART

An orthodiagraphic study of 291 male students at the University of Pennsylvania, between the ages of 16 and 26 years, with no evidence of cardiovascular disease, made by J Edeiken and F C Wood,1 suggests that the predicted cardiac area of J A E Eyster and F J Hodges (1926) is approximately 10 per cent too high and the predicted transverse cardiac diameter 0.5 cm too long for young male adults The cardiothoracic ratio in 853 per cent of the students was between 040 and 050. 83 per cent showed ratios slightly above and 62 per cent slightly below these figures Hearts which were small in the frontal plane frequently had a small anteroposterior diameter The shape of the heart was found to vary greatly (Fig 12), being influenced by (a) physique, (b)height of diaphragm, (c) shape of chest, and (d) spinal curvature

In the vertical or ptotic heart, the region of the pulmonary artery was frequently prominent, when combined with a straight left border, it sometimes simulated a "mitral heart" Right scoliosis may produce the so-called mitral configuration, and may also make the aortic knob more readily visible by removing the some from the background scoliosis may cause the supracardiac shadow to appear widehed, as it displaces the descending aorta to the left Rotation of the individual to the left in right scoliosis, and to the right in left scoliosis, tends to correct the picture and may show the heart to be of normal shape. In many cases the shadow of the proximal portion of the descending aoita could be seen above the heart

No rigid roentgenological criteria can be relied upon to determine the presence or absence of heart disease. Any single measurement, when used alone, may be misleading. In each case the area of the silhouette, the transverse diameter, the cardiothoracic ratio, the anteroposterior diameter, and the shape of the heart should be given consideration

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XIII. TOTAL THYROIDEC-TOMY IN TREATMENT OF HEART DISEASE

Since the introduction of thyroidectomy as a method of treatment of severe congestive heart failure in patients with for the lessened needs of a reduced metabolic rate — considerable has been written in regard to the limitations and value of the procedure.

An estimation of the value of total thyroidectomy in the treatment of con-

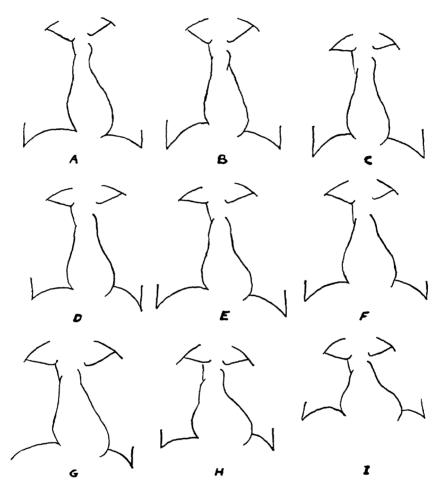


Fig. 12—Showing the various heart shapes encountered in 291 college students without evoletics of cardia vascular disease. The heights and weights of the different individuals are as to lows: (1) its inches 127 pounds: (B) ith inches 130 pounds: (C) ith inches 122 pounds: (D) 70 piches 158 pounds: (I) its inches 148 pounds: (I) 70° inches 124 pounds: (G) 70 inches 130 pounds: (H) its inches 145 pounds: (I) 70° inches 192 pounds: (Fdeiken and Wood. Am Heart I. Apr. 1937.)

normal metabolism by H. L. Blumgart, S. V. Levine and D. D. Berlin¹—on the theory that the hearts of such individuals might be unable to supply enough blood for the ordinary demands of a normal metabolic rate, but might, nevertheless, be capable of supplying sufficient blood

gestive heart failure and for the relict of angina pectoris is presented by W. H. Parsons and W. K. Purks² on data obtained through a survey of the literature and from an inquiry sent to all members of the American, Southern and Western Surgical Associations, the

American Association for the Study of Conter, and a number of other American clinics. Information was obtained on 229 patients operated on for congestive heart failure and 133 patients operated on for the relief of angina pectoris In 291 cases there were data on complica-Tetany, which occurred in 103 per cent, was of a transient character in all but one case in which it was the cause of death Injury to the recurrent laryngeal nerve, which occurred in 82 per cent, was in no instance bilateral It seems that serious or permanent complications are not sufficiently frequent to rule against the procedure

In the group with congestive heart failure, the operative mortality was 10 48 per cent. Excellent results were obtained in 34 63 per cent, moderate improvement in 28 78 per cent, slight improvement in 2 92 per cent, and no improvement in 33 65 per cent. In the angina pectoris group of 133 cases, the operative mortality was 3 7 per cent, excellent results were obtained in 55 46 per cent, moderate improvement in 28 12 per cent, and no improvement in 12 5 per cent.

The authors conclude that there is slightly more than 50 per cent chance of satisfactory improvement in cases with congestive heart failure and somewhat better than 75 per cent satisfactory results in angina pectoris, they admit inability to answer the question whether operation prolongs lite. It is admittedly only a form of symptomatic treatment which in no way alters the underlying cardiac pathology. We must bear in mind that we are treating one disease by substitution of another, even though the latter, myxedema, is milder and more amenable to treatment."

In the discussion of the paper, Dr F H Lahey stated that his experiences

with 27 cases who have been carefully followed has not been gratifying He does not believe that this procedure will endure because these patients have a very limited cardiac reserve, and myxedema is an undesirable state for a decompensated heart. In his mind the majority of cases will return to decompensation later. In a few cases of angina pectoris, however, better results were obtained, and, therefore, if a patient is willing to exchange an active state for the sluggish state of myxedema, there is a possibility that anginal pain can be reduced Total thyroidectomy is a difficult operation, demanding the highest degree of technical skill

Improvement in the results of this surgical procedure will depend on a careful selection of patients. The operation is contraindicated in the presence of bacterial or rheumatic carditis, renal insufficiency, cirrhosis of the liver, or the presence of a recent coronary occlusion. It is doubtful whether anything can be accomplished in the rapidly progressing cases that do not show any improvement on prolonged rest in bed and medical therapy, and in cases with a low basal metabolic rate.

Enough clinical improvement has been obtained in a sufficient number of cases of congestive heart failure and even more in angina pectoris to justify total thyroidectomy as an advance in the treatment of this type of heart disease. However, as stated by Parsons and Purks, "it is imperative that the accessibility of this procedure should in no wise lessen our attempts to control all cardiac problems by nonsurgical means."

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XIV. TREPOPNEA (TOLER-ANCE OF CERTAIN CAR-DIAC PATIENTS FOR VARIOUS RECUM-BENT POSITIONS)

Observations in regard to trepopnea (the ability of certain cardiac patients to rest comfortably in one recumbent position—with intolerance for another) have been made by F. C. Wood and C. C Wolferth¹ in a study of 52 cardiac patients (32 with trepopnea of preference

symptoms experienced in one horizontal position and relieved by assuming another are dyspnea and precordial discomfort, cough and anginal pain are less frequent; fatigue, dizziness and palpitation also occur. With this syndrome there is usually present considerable cardiac enlargement with definite reduction in functional capacity. As the clinical condition of the patient changes, symptoms may change in intensity. No apparent correlation between the position the in-

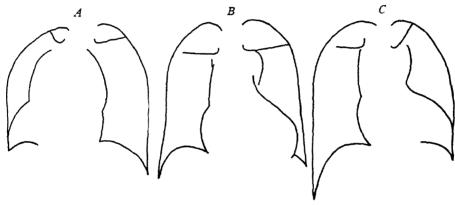


Fig 13—Orthodiagrams of a patient with degenerative heart disease and trepopnea of choice, showing marked movement of the heart, and definite change in shape of the supracardiae shadow, with change of position A. Patient lying on right (best position). Heart against the right chest wall. Supracardiae shadow II cm. in width B. Patient erect. Supracardiae shadow 7.5 cm. in width C. Patient lying on the left (worst position). The heart has moved 6.5 cm. to the left, when compared to A and is now resting on the left chest wall. The supracardiae shadow is 7.8 cm. in width. The movement of the heart in this patient was about as great as any we have seen. (Wood and Wolferth. Am. J. M. Sc., March 1937.)

and 20 with trepopnea of necessity). Certain patients in severe congestive failure could not tolerate recumbency in any position very long, but did have a definite preference for one over another, a few were intolerably dyspheic in all horizontal positions, with no preference, both types were most comfortable sitting up, though not necessarily free from dysphea Finally, some individuals with marked congestive phenomena could lie comfortably in all recumbent positions.

Usually patients prefer the right side and dislike the left, but many variations are encountered. The most common

dividual prefers and any known cardiovascular characteristic, such as type of lesion, type of failure, or shape of heart, has been demonstrated. Observations of patients in their unfavorable recumbent position show that the dyspinea is probably a subjective phenomenon—a sense of suffocation—which may or may not be accompanied by obvious increase in rate or depth of breathing (a fact also true of orthopnea)

Roentgenolgic study shows that the heart may move considerably as a patient changes from one side to the other (Fig. 13), that the intensity of symp-

toms is not proportional to the distance the heart moves; that the shape of the heart and aortic arch may change markedly as the individual changes position; and that, with the patient in lateral decubitus, the heart is lifted during each inspiration, sometimes a distance of several centimeters. The vital capacity does not tend to be greater in the most favorable recumbent position than in the one least tolerable.

Patients with marked trepopnea do not assume their most unfavorable position at night, even when sleeping. Those in whom it is less severe are sometimes found in an unfavorable recumbent position during sleep, although they may deny that this position can be tolerated Studies of the pulse, the arterial pressure, the cervical veins, and the heart sounds have not as yet afforded helpful One individual without information heart disease or preference for any particular recumbent position showed a lower cardiac output on the left than on the right. The change of position of the heart under the influence of gravity, with distortion of the large vascular channels in the mediastinum, is suggested as a possible cause for this phenomenon

In a subsequent publication, F (Wood C Wolfeith and A W Teirell? discuss trepophea as an ethological tactor in paroxysmal nocturnal dyspnea Practically all cases of paroxysmal nocturnal dyspinca have a predisposing tactor giving rise to an actual or latent tailure of proper blood flow from the lungs to the aorta—which may be (a) left ventricular failure. (b) mitral valve obstruction, or (c) any other condition which might interfere with the flow of blood from the lungs In addition, a precipitating factor, capable of producing a sudden intensification of this failure of proper blood flow from the lungs to the aorta seems necessary,—this may be (a)

the assumption of an unfavorable recumbent position during sleep (orthopnea or trepopnea), (b) a dream which gives rise to emotional disturbance or to physical effort, or in occasional cases the onset of a paroxysm of arrhythmia or a coronary occlusion Conditions which may exaggerate the predisposing factor or facilitate a precipitating factor are hot weather, abdominal distention (stomach, bowels or bladder), respiratory infection, and undue physical or emotional activity during the day Furthermore, a low serum protein or an allergic tendency may increase the respiratory distress of an attack by superimposing pulmonary edema and bronchospasm

Many individuals with trepopnea do not experience paroxysms of nocturnal dyspnea On assuming an unfavorable recumbent position during sleep, some patients are awakened by symptoms other than dyspnea, especially pain, palpitation and cough, others are able to avoid their unfavorable position unconsciously without awakening If a trepopneic individual becomes unconscious or paralyzed, the responsibility for avoiding unfavorable position may devolve upon the physician and nurse. In case an individual subject to attacks of paroxysmal dyspnea assumes a certain recumbent position during sleep, he might be prevented from doing so by being fitted with a fairly snug woolen undershiit with large wooden spools sewed to those sides which should be avoided

Patients with mild degrees of trepopnea usually are capable of sleeping in their most unfavorable recumbent positions. However, if further impairment of blood flow from the lungs to the aorta occurs, either temporary or permanent, the assumption of an unfavorable position during sleep may initiate a severe attack. The demonstration that trepopnea is a precipitating factor in paroxysmal nocturnal dyspnea supplies an explanation for the onset of attacks in certain cases in which formerly no adequate cause was recognized

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XV. TREATMENT

1. Left Ventricular Failure

In heart failure resulting from hypertension, sclerosis of the coronary arteries, syphilitic aortitis, and diseases of the aortic valve, the dominant effect is on Failure of the left the left ventricle ventricle before failure of the right ventricle results in pulmonary congestion with perhaps little or no engorgement of the peripheral veins, and may give rise to paroxysmal dyspinca (cardiac Shortness of breath on exerasthma) tion may for months be the only subjective symptom of left ventricular failure, in some instances angina pectoris is the first manifestation, and in others there is a history of severe and lasting anginal pain indicative of coronary thrombosis. Occasionally paroxysmal dyspnea is the first intimation of cardiac disease under these circumstances usually being the result of coronary thrombosis. The attacks may occur during the day tollowing exertion or excitement, but later in the course of the cardiac disability they usually occur at night, awakening the individual from sleep

Harrison and his co-workers point out that various factors, such as cough, nightmares or dreaming, abdominal distention, and the desire to urmate may precipitate nocturnal attacks. Coughing, incident to the pulmonary congestion, and perhaps the associated bronchitis, is the most common exciting agent. It produces a

marked increase in the respiratory rate which accelerates the return of the venous blood to the right side of the heart, which in turn aggravates the pulmonary congestion, thereby promoting the possibilities for the continuation of the cough-A vicious cycle may be instituted which, unless interrupted, may progress to pulmonary edema and end fatally Apprehension deserves particular eniphasis as a factor which may contribute to the onset and progression of the attack, possibly through an elevation of blood pressure. It is important to keep in mind that an abrupt increase in the already existing pulmonary congestion is primarily responsible for the paroxysmal dyspnea, regardless of the nature of the exciting agent

Structural alterations of the heart are usually apparent from the increase in the size-particularly involving the ventricle, the presence of gallop rhythm and possibly a systolic apical murmur. The intensity of the pulmonary second sound is commonly accentuated, more especially during attacks of paroxysmal dyspical because of the increased tension of the pulmonary circulation. Pulmonary congestion is a prominent feature, generally evidenced by moist, sibilant and musical râles, but not apparent on x-ray examination. The reduction in the vital capacity reflects the extent of the pulmonary congestion and also serves as a valuable guide in following the results from treat-In the more severe attacks the evanosis and particularly the ashen gray color, profuse cold perspiration and pulmonary edema are conspicuous teatures. The cardiac rate is invariably accelerated and the blood pressure generally clevated above the usual level

Treatment-In discussing the treatment of left ventucular failure, F. M. Smith1 states that minor nocturnal attacks are usually aborted by assuming the

upright position; but that more severe attacks constitute a major cardiac emergency, demanding prompt and energetic treatment Morphine sulfate, 1/4 grain (15 mg), is the most effective remedy, and should be administered immediately and repeated if necessary It curtails the demands on the left ventricle by eliminating anxiety and restlessness and their effect on the blood pressure; in addition it depresses the respiratory center, thereby suppressing coughing Theophylline with ethylenediamine, $7\frac{1}{2}$ grains (0.48 Gm), in from $1\frac{2}{3}$ to 3^{1}_{3} ounces (50 to 100 cc) of 50 per cent dertrose solution administered slowly intravenously is also very effective in preventing and abolishing attacks results of the latter are attributed to the favorable action on the coronary circulation and the resulting increased efficiency of the left ventricle. The hypertonic dextrose solution is believed to enhance the effect of theophyllme with ethylenediamine on both the heart and the pulmonary congestion. Digitalis in the form of digifoline, 30 to 60 minims (2 to 6 cc), is often administered with the preceding in order to produce the maximum effect on the left ventricle Intramuscular or intravenous administration of ouabain, 11.5 grain (0.5 mg + or amorphous strophanthin, 165 giam (1 mg), is often recommended because of the prompt and powerful action. The latter drugs are dangerous if given in larger doses or if digitalis has been taken beforehand

Venesection is a valuable measure, especially in the plethoric type of individual, the rapid withdrawal of blood (500 cc) reducing the venous return to the right side of the heart and thereby decreasing the pulmonary congestion. It also diminishes the load on the left ventricle through reduction in the blood pressure and the viscosity of the blood

Similar effects may be obtained by the procedure termed *venestasis*, in which the reduction of the venous return to the right side of the heart is effected through trapping the blood in the four extremities by the application of the cuff of a clinical sphygmomanometer as high up as possible on each of the extremities and inflation to pressure of from 60 to 80 mm of mercury. With the subsidence of the attack, pressure may gradually be decreased from one extremity at a time

If the attack continues after the preceding, the administration of oxygen should be instituted by nasal catheter, if a tent or oxygen chamber is not available. With excessive elevation of blood pressure, the use of glyceryl trinitrate is indicated because of its effect on arterial tension and action on the coronary circulation. It is doubtful whether atropine has any significant value, and the administration of epinephrine is not advisable in disease of the coronary arteries.

Subsequent Treatment—This consists of

- 1 "Bed rest for from four to six weeks with complete relaxation and adequate sleep
- 2 "Simple diet with plenty of carbohydrates
- 3 "Regulation of the bowels by simple measures such as the administration of *liquid petrolatum*
- 4 "The administration of theophylline and ethylenediamine from 0 1 to 0 2 Gm (1½ to 3 grains) from three to four times a day, digitalis (powdered leaf) 0 1 Gm (1½ grains), three times a day, for from five to six days and thereafter once a day, and the use of a mercurial diuretic if necessary to eliminate the pulmonary congestion
- 5 "Later the elimination or the control as far as possible of factors promoting the cardiac disability, and finally the careful extension of the physical activities"

Adequate sleep is essential to the restoration of the cardiac function and is best obtained by the use of morphine for the first few nights Thereafter simple sedatives, particularly when supplemented by theophylline with ethylenediamine, will produce the desired sleep and aid in the prevention of the attacks Theophylline with ethylenediamine, usually administered in 50 per cent dextrose solution, is more effective when given intravenously shortly The oral administrabefore bedtime tion of theophylline with ethylenediamine is generally employed and continued indefinitely Digitalis is necessary with auricular fibrillation, and its use $_{10}$ 1^{1} /₂ gram (0.1 Gm) doses daily is advisable with normal cardiac mecha-The restoration of the heart to the maximum efficiency calls for a long period of rest followed by gradual and carefully supervised extension of the physical activities. The patient should not be permitted to be up and about until long after the pulmonary congestion has disappeared Determination of the vital capacity at weekly intervals provides a valuable means of following the course of recovery. In the more advanced cases the use of salyrgan, perhaps preceded by the administration of ammonium chloride, may be necessary to eliminate the pulmonary congestion

2. Action of Drugs on the Heart and Circulation

A clinical study of the action of ten commonly used drugs on cardiac output, work and size, on respiration, on metabolic rate, and on the electrocardiogram has been made by I Starr, C J Gamble, A Margolies, J S Donal, Jr, N Joseph and E Eagle ² Cardiac output was estimated by the *ethyl iodide method* and correlated with heart volume, calculated from the surface area. For a

given amount of work done, myocardial efficiency varies inversely with the diastolic volume of the heart Cardiac stimulation was therefore measured by increase in work, by an increase in the ratio "work per beat/diastolic volume."

In all cases of cardiac disease (free of congestion, but evidently having early failure), the heart was stimulated by digitalis, while in normal individuals after a transient increase there was a reduction in cardiac output following digitalis administration. Adrenalin. and to a less degree ephedrine, caffeine and theophylline with ethylenediamine, were found definitely to stimulate the heart and respiration; the mean blood pressure was not appreciably altered by any of them. Three of seven patients given theophylline had angina pectoris, but in spite of the increased heart work following the administration of the drug, no cardiac pain re-The studies showed that caffeine and theophylline rank among the most powerful cardiac and circulatory stimulants

Carbaminoylcholine (doryl), whose action is similar to that which follows stimulation of parasympathetic nerves, gave rise to a significant increase of pulse rate and respiration, and significant diminution of blood pressure and peripheral resistance, without any significant change in cardiac output When the blood pressure was lowered rapidly by a nitrite, the cardiac output was regularly increased, if the blood pressure fell slowly or not at all, the results were less regular, either an increase or no change being found Cardiac work per minute diminished, not significantly, after sodium nitrite, but apparently increased in two experiments after nitroglycerine. No significant change in any item measured followed the administration of pitressin. The average results

did not demonstrate cardiac depression with *quinidine*, although larger doses than usual were administered.

Morphine caused no change or very small reduction in pulse and respiratory rate and basal metabolic rate, diminution of cardiac work after morphine was somewhat more obvious in the cardiac cases, though absent in the more nearly normal individuals Strychnine in a dose of 18 mg (about ½0 grain) was found to have a mild vasoconstrictor effect, but no cardiac or respiratory stimulant action was observed

3. Efficacy of Various Digitalis Preparations

The results of a six year clinical study of the efficacy of six digitalis preparations have been reported by W. D. Stroud and | B Vander Veer 1 The various preparations, viz., (1) whole leaf tablets of digitalis prepared by the American Heart Association, (2) Burroughs, Wellcome & Company whole leaf tablets, (3) digalen a preparation of glucosides" (Hottman-La-Roche Inc.), (4) verodigen, a gitalin glucoside (Merck & Company), (5) digitaline (Nativelle), and (6) digovin, a glucoside isolated from the leaves of digitalis lanata (Burroughs, Wellcome & Company), were prescribed to ambulatory patients in the adult cardiac clime of the Pennsylvania Hospital There were 47 cases of chronic auricular fibrillation, three with auricular flutter, and six with normal sinus rhythm with congestive heart failure. Each preparation was administered for a period of nine months to one year. At intervals of from one to four weeks each patient reported for checkup of symptoms and a physical examination, including a vital capacity determination Electrocardiographic and orthodiagraphic studies were made every three or four months In Table four are

TABLE 4

Doses of Various Preparations

| Name of Preparation | One Cat Unit, Grains | Full Digi- talization, Grains |
|---|---|---|
| American Heart Association whole leaf tablet Burroughs, Wellcome & Co whole leaf tablet Digalen Verodigen Digitalin (Nativelle) Digoxin | 1½ 1½ 1½ 1½ 1/240 1/600 1/160 | 18-30 18-30 18-30 1/20-1/12 1/50-1/30 1/13-1/8 |

listed the clinical equivalent of approximately one cat unit of each preparation and the average full digitalization dose given over a period of from three to six days. All the preparations were uniformly potent and efficacious, producing similar results when given orally in equivalent doses. There was no evidence that the glucoside preparations, when given by mouth, were quicker in action, more efficient, more prolonged in action, or less toxic than standardized whole digitalis leaves.

4. Urginin in Treatment of Myocardial Insufficiency

In a clinical study of the effects of urginin (a preparation of squill)—consisting of a mixture in approximately equal proportions of two of the active, water-insoluble glucosides, crystalline scillonin A and amorphous scillonin B, derived from Urginea Maritima-made by F. L. Chamberlain and R. L. Levy⁴ on 62 patients in the wards of the Presbyterian Hospital, New York City, it was found that the drug administered orally exerted an action on the heart like that of digitalis in cases of cardiac insufficiency. In terms of cat units, the therapeutic potency of urginin is about one-half that of digitalis This difference in activity may be ascribed to less complete absorption or more rapid elimination of urginin. When no urginin or digitalis has been given for at least ten days preceding, a satisfactory scheme of dosage is as follows 15 mg (3 tablets). three times a day after meals for two days, and then 10 mg (2 tablets), twice daily, until the desired effects are pro-The daily maintenance dose duced ranged from 0.5 to 20 mg, the average being 0.92 mg (approximately 170 grain)

In cases of auricular fibrillation, the effect on ventricular rate began to dinumsh in three to ten days, disappearing completely in from 8 to 11 days, after stopping the drug Changes in the form of the electrocardiogram were observed for as long as 17 days after the drug had been discontinued. Prolonged X-V conduction was recorded from 3 to 16 days after the last dose. Premature beats as evidence of intoxication were not In ten patients premature observed beats disappeared after medication six patients nausea and vomiting occurred soon after urginin was taken, in nine additional patients nausea without counting occurred, in each instance smaller doses were tolerated without distress. Other toxic effects observed were diarrhea (two cases), dizziness and flushing (two cases), mental confusion (one case), transient auricular fibrillation (two cases), auriculoventricular nodal rhythm (three cases), prolonged P-R interval (six cases), and A-V heart block (three cases). One patient nauseated by digitalis took urginin without distress, another had diarrhea after taking digitalis, but none following No deaths could be urginin therapy attributed to the action of urginin

Urgmin appears to be an effective cardiac remedy, however, it offers no advantages over digitalis in the treatment of invocardial insufficiency. It seems that for the present the indication for urginin niight be in those patients who because of an idiosyncrasy or prejudice are unable to take digitalis with out unpleasant effects.

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ENDOCRINOLOGY

By CHARLES W. DUNN, M.D.

ADDISON'S DISEASE AND SUPRARENAL **INSUFFICIENCY**

1 W Spence 1 states the fundamental cause or death in Addison's disease is deficiency of the adrenal cortical secretion. The lesions causing the destruction of the adrenal cortical cells are tubercular in 70 to 90 per cent of the cases Atrophy of the adrenal gland is the next most frequent cause. It is not exclusively an adult disease, as it occurs at any age of life in both sexes, but it is

most frequent between the ages of 30 to 50

Adrenal cortical deficiency accounts tor most of the clinical findings, how ever the pigmentation, hypotension, and hypoglycemia are probably or medullary origin

Three stages are usually defined (1) The early or latent phase, which is difficult to diagnose, (2) the Addisoman syndrome, (3) the collapse or terminal stage

Larly symptoms include nausca, vomiting, epigastric discomfort,

loss of weight, asthenia, depression, and insomnia. The gastrointestinal disturbances are usually prominent in children.

Pigmentation may be the only sign. It appears on the sun-exposed areas, on areas of the body which are subject to the pressure of clothing, or it is evidenced by an increase of the normally pigmented areas. Axilla, areola of the nipple; linea alba, the genital and anal regions. Or it may appear about the buccal mucous membrane, or as discrete areas, as dark brown or black pigmented spots or freckles. In acute cases of Addison's disease it may not occur.

The body temperature is subnormal; they are susceptible to colds and infections, and have poor resistance to operations and shocks. The heart is frequently diminished in size, the sound is faint and distinct, the systolic pressure is usually lower than 90 mm of Hg, but early in the disease, the blood pressure may be increased.

The chronic type is characterized by remissions and relapses, during the former, which may vary from weeks to years, while many features of the disease improve, the blood pressure commonly remains low-a crisis may occur at any time and is heralded by increasing weakness, psychical disturbances, deepening of pigmentation, nausca, vomiting, fall of blood pressure and temperature. Since crises are characterized by severe nausea and vomiting, marked loss of weight, and systolic blood pressure of 70 or below, and possible suppression of urine, it is in this state of collapse and dehydration that death usually occurs

The prognosis is best in those "who eat and gain weight," and in those with marked pigmentation, little asthenia, and few gastrointestinal symptoms

The clinical condition can be gauged by the level of blood sodium (normal: 325 mg. per 100 cc. of serum). The

more severe case excretes excessive amounts of sodium Blood potassium (normal: 20 mg per 100 cc. of serum) rises; a high potassium value is the most reliable chemical indication of the seriousness of adrenal cortical deficiency A high or rising blood urea also indicates a serious condition is present or imminent

Due to the dehydration, the serum proteins (normal · 5 6 to 8 5 Gm per 100 cc of serum) rise, but in the presence of this blood concentration the blood sugar usually falls—a level of 60 mg per 100 cc. of blood is a serious, and often a terminal, event The normal blood calcium is generally 9 to 11 mg per 100 cc of blood

The gastric juice analysis usually shows hypochlorhydria or achlorhydria The B M R is usually low—minus 18, and x-ray examination of the adrenals may reveal calcification

Diagnosis — Pigmentation of the mouth, if other causes are excluded, is of diagnostic importance. The abdominal pains, unless associated with tenderness in the loins, may simulate other abdominal lesions, such as carcinoma of the alimentary tract, peptic ulcer, and renal disease. Other conditions which must be excluded are. Pernicious anemia, chronic nephritis, apathetic toxic goiter, essential hypotension, Simmond's disease, myasthenia, gravis neurasthenia, and menopausal states.

X-ray of the alimentary tract and tests for fecal occult blood are valuable aids when lesions of the gastrointestinal tract are suspected

Conditions such as diabetes mellitus and high intestinal obstruction often cause acidosis, and in this state low blood sodium also occurs. Consequently, this finding, which is usually present only in chemical change in early or chronic cases, is not pathognomonic.

In doubtful cases of Addison's disease, the use of a salt-free diet generally ex-

acerbates the signs of Addison's disease, even to precipitating a critical state

Treatment — The general principles include: Protection from cold, shock, and exertion, by rest in bed; a high carbohydrate diet with a low potassium content, and vitamin C in adequate amounts.

In early and chronic cases, 2 to 3 Gm (30 to 45 grains) of sodium chloride are given in milk six times daily. If nausea results from the large amount of salt taken, a mixture of sodium salts 6 Gm (90 grains) of sodium chloride, 4 Gm (60 grains) of sodium bicarbonate, and 4 Gm (60 grains) of sodium citrate—is administered. This therapy usually relieves the asthenia and gastrointestinal symptoms, and increases the weight—and possibly the blood pressure, but has no effect on the pigmentation.

The sodium therapy generally diminishes the amount of adrenal cortical extract required, but some cases will not respond to salt therapy, and require cortical extract

During crises, cortical extract is required—50 cc of the standardized cortical extract is injected intravenously. The dosage is progressively reduced 10 cc daily as the clinical condition improves. After the first week the extract may be given intramuscularly. With response to cortical extract therapy, nearly all the symptoms and signs except the pigmentation disappear. The blood chemistry returns to normal values, with the exception of the hypoglycenia.

As the patient's health is restored and weight gain is established, the dosage of adrenal cortical extract is reduced to 1 to 5 cc twice daily, salt therapy is continued

In spite of the dramatic and enthusiastic results, there are cases—those of pro-

tracted crises, and those of chronic or stationary periods of the disease—which do not respond even to large doses of cortical extract.

Dehydration and hypoglycemia are held by many to be largely responsible for the symptoms of the crises. To combat this, 500 cc of a five per cent solution of glucose—in five to ten per cent solution—is administered to prevent the occurrence of rigor, and is repeated when necessary during the next few days. Since the adrenal cortex prevents the loss of fluids from the body, it should be administered intravenously before or during the administration of the saline-glucose solution.

Acute adrenal insufficiency results from acute infections, thrombosis of the adrenal vessels and bilateral hemorrhage of the adrenal glands

Suprarenal hemorrhage may occur in the newborn as the result of eclampsia, birth trauma, asphyxia neanatorum, and superinvolution of the cortex; in older people, the more frequent causes are Hemorrhagia, diasthesis, extensive burns, severe infections, and syphilis. In the newborn it is often described as pseudopneumonia because of the acute onset of the high temperature, dyspnea, cyanosis, but in the violently acute ill infant, the absence of pulmonary signs should arouse suspicion of adrenal hemorrhage In older children and adults, the gastrointestinal signs and fever are prominent All ages exhibit extreme asthenia, prostration and low blood pressure, dehydration, convulsions and coma. A palpable mass in the region of the kidney is often recognizable, and abdominal distension is present with the signs of collapse and shock

The therapy consists in the administration of cortical extract and glucosesaline solution, and the usual shock therapy.

Chronic adrenal insufficiency is not well defined. The clinical signs are Debility, emaciation, hypotension, impotence, and a low basal metabolic rate—and are usually defined as such. In the majority of such cases it is doubtful whether adrenal cortical lesions be present, consequently, they experience little relief from the administration of adrenal cortical extract.

Kline² describes the effect of sodium chloride restriction in a case of Addison's disease. The reduction of sodium chloride intake may manifest its effect on the first day, but more frequently appears from the third to fifth day.

The patient was receiving 3 drams (12 (m)) of sodium chloride in his diet, which was reduced to 21.6 grains (1.4 Gm) daily. On the fifth day the typical Addisonian crisis appeared, the blood nonprotein nitrogen rose from 35.2 mg to 48 mg, and the plasma chlorides fell from 326 mg to 284 mg with a plasma sodium of 224 mg per 100 cc of blood.

Wilder et al have shown that even in the presence of a high sodium chloride (188 mg) in the diet, a crisis can be induced by a high potassium content of the diet. Consequently, in the salt therapy of Addison's disease a high salt diet also requires a low potassium intake for successful therapy, and conversely, in the salt deprivation diet for diagnostic purposes an increased potassium diet is essential

ADRENAL HEMORRHAGE IN CHILDREN

Firor³ reports extensive adrenal hemorrhage found in over 20 autopsies, and adds the case of a 13-months-old infant in whom the real nature and progress of the illness was not apparent until the postmortem examination was completed.

The onset was an unexplained 104° F (40° C) temperature which persisted for two days. Three days later he suddenly became pale, exhausted and restless. The following morning a bloody stool was observed. The next morning, after admission to the hospital, another bloody type stool occurred.

The physical examination showed a sallow, slightly undernourished infant who was alert and, apparently, not acutely ill. Hb was 55 per cent, R B C 4,300,000 and W B C 9600 with 67 per cent lymphocytes and abundant platelets

Complete examination of the systems revealed no etiological factor The infant remained well for one week, and the Hb rose to 67 per cent. He then became listless, and the next day two tarry stools were expelled and the Hb fell to 50 per cent, but the following day the stools were normal. No abnormal mass or tenderness of the abdomen was palpable He remained in the hospital Occasionally he would draw his leg up under him and cry as though in pain. Since episodes of bleeding recurred and the Hb had at one time fallen to 20 per cent, an abdominal exploratory was made, which chiefly revealed transverse bands over the descending colon, some thickening of the transverse colon, and enlarged mesenteric lymph nodes. The bands were released and the appendix removed

An unexplained temperature of 106° F (411°C) occurred some time after the operation that remissed to 102° F (388°C) the following morning and at 8 P M rose to 107° F (417°C) following seven fluid nonbloody stools that afternoon. The next day sudden circulatory collapse and death occurred despite adequate (intravenous) therapy

The two unexplainable conditions, intestinal bleeding and a fatal circulatory collapse with pyrexia, were explained by

the autopsy. An infected cavity in the pancreas communicating with the pancreatic duct explained the bleeding into the gastrointestinal tract, and extensive hemorrhage destroying both adrenal glands accounted for the collapse and death of the infant.

The adrenal glands were of equal size, and together weighed 10 Gm. The cut surface showed a reddish cortex which was almost destroyed by the hemorrhage

The analysis of records of over 20 cases of extensive adrenal hemorrhage in infants and children permits classification into two groups (1) Hemorrhages in the newborn, and (2) those associated with infections

Hemorrhages of the newborn usually appear a few days following birth, and are sometimes diagnosed by the bilateral palpable hematoma in the adrenal and kidney region. Because of the rapid respiratory rate, Goldzieher suggested the name pseudopneumoma infantium, especially because of the unexplained pyrexin and negative lung findings.

The cause of these hemorrhages is not due to infection or trauma but probably to an exaggeration of the normal physiological involutional process occurring in the androgenic zone.

The second group of adrenal hemorrhages composes those associated with infections, such as from meningococcus occurring in the Waterhouse-Frederichsen syndrome. In some meningococcal infections, the infection is so tulnimating that patechial hemorrhages in the skin and viscera occur.

In none of the above cases was the diagnosis of adrenal hemorrhage made during life all had high fever (104) to 107. F. [40] to 41.7. C.[1], sudden circulatory collapse, and died

Many explanations of the cause of the destructive hemorrhage have been advanced, as venous thrombosis, spasticity

of the unusually thick musculature of the adrenal veins, bacterial toxins, and altered cell-permeability

Diagnosis — There are no tests to diagnose this condition, the presence of unexplained hyperpyrexia in cases of infection due to a toxin producing bacteria is the signal for alertness in diagnosis of adrenal hemorrhage.

The only therapeutic procedure suggested is operation and evacuation of the clots, as performed by Corcoran and Strauss,⁴ and the administration of a potent cortical extract

THE ADRENOGENITAL SYNDROME

Definition—L R Broster⁵ defines the adrenogental syndrome as that condition in which secondary male sex characteristics appear in the female Associated with a retrogression of the primary and secondary feminine sex characteristics and their functions

The clinical syndrome is produced by pathological changes. Hyperplasia, adenoma or malignancy of the adrenal gland. The effects of the lesion will vary according to whether the patient is an immature or a fully developed individual at the time of onset of the adrenal cortical disorder.

The ages of the patient and the type of pathology determines the rapidity of the appearance, the progression of the clinical symptoms and the prognosis. Malignant forms are usually rapidly tatal.

Classification — Broster's classification of the adrenogenital syndrome is

1 Idrenal pseudohermaphroditism which represents the most complete form of the syndrome in that the changes occur before the body form and sex organs have become differentiated. Marked virilism, masculine hypertrichosis, primary amenorrhea and absence of normal tem-

inized development are present in pseudohermaphroditism.

2 Adrenal virilism occurs when the adrenal changes have their onset after puberty. This type is distinguished by the alterations in the body form and in the external sex organs, the disturbance of sex function and the male type of hypertrichosis. The disturbed sex gland physiology is expressed by regressive changes: Bodily changes toward masculinity, diminished menstrual flow and a diminution in the size of the breasts.

There occur a relatively large number of cases in this group who present mild hypertrichosis with or without slight changes in the menstrual rhythm. Some of the above cases might be described as instances of familial hypertrichosis.

- 3 The Achard-Thiers syndrome or the "diabetes of bearded women" presents the symptom complex of obesity, glycosuria and decreased sugar tolerance, hypertension, usually amenorrhea, and facial hypertrichosis of the male type but without other signs of virilism
- 4 Postmenopausal virilism, which is associated with hypertrichosis apical baldness, enlargement of the clitoris, and a tendency toward obesity

Symptomatology - Hypertrichosis-The male type of hair varies from the curly, crisp variety to the soft downy type, which is patchy. It occurs on the face in the form of 'mutton chop" whiskers, mustache or beard trunk it appears as a halo around the nipples, it may cover the midsternal, the shoulder and lumbosacral region and extend triangularly from the umbilicus to the pubis (male escutcheon) The axilla and perineum are densely covered Heavy growth of hair occurs on the extremities, especially the thighs, legs and forearms The male mimicry may even extend to the dorsa of the feet or on the proximal

phalanges In older women, apical baldness and temporal recession may be conspicuous.

Changes in Bodily Contour—These changes vary with the time of onset and the degree of virilism. Individuals in whom virilism develops early are short, thick-set, broad shouldered, deep chested and narrow hipped. The muscles of the extremities stand out prominently under the coarse dark skin and the diminished fat—when feminine growth has been established the bodily contour changes are less marked and consist of a lessened disproportion between the relative breadth of the shoulder and pelvic girdles and a suggestion of undue prominence of the superciliary ridge or jaw.

The breasts may be: Absent, underdeveloped, the mature type of breast exhibiting regression changes, or are enlarged due to obese deposits

A few cases have shown some enlargement of the larynx but in a larger proportion the pitch of the voice is altered, being deeper in tone and rough or husky

Changes in the Female Genitalia—
These comprise enlargement of the male elements and diminution of the female ones. The clitoris is invariably enlarged and when notably enlarged it shows a groove on its under surface. The labia are small and underdeveloped. The uterus is diminished in size and the ovaries exhibit degenerative changes. Ovaries which may be enlarged to the size of a golf ball have been observed. They are of pale color, fibrotic and studded with small cysts, more rarely a small and fibrotic and even a calcareous ovary is found.

Disturbances in Sexual Function— Primary and secondary amenorrhea occur The latter is more common and has its onset at or soon after the appearance of the hypertrichosis Changes in the Psychologic Outlook—\ fairly high percentage of nervous and mental illness exists among these patients. They are heterosexual, homosexual or narcissistic

Differential Diagnosis — Arrhenoblastoma of the ovary, tumor of hypothalmus and Cushing's syndrome must be differentiated from the adrenogenital syndrome

Laboratory Investigations — These have given mainly negative results. The pituitary fossa is invariably small, while the injection of an iopax medium and subsequent x-ray may show a distortion or relative displacement of the renal pelvis on one side, thereby suggesting an adrenal gland tumor. Exploratory laparotomy is the only reliable method of determining the relative size of the adrenal glands or the presence of accessory adrenal cortical masses and uterine and ovarian changes.

Therapy — Unilateral adrenalectomy in these patients has shown no untoward sign so far as the general physical condition and well being are concerned in general, there has been a definite tendency toward restoration of the menstrual function Oestrin injections improve the more obstinate cases of impaired menstrual function

Postoperatively it is possible to pull out bunches of acquired hair. The hair regrows but gradually loses its virile characteristics.

"The lett adrenal has been more frequently excised. The other adrenal gland may hypertrophy. This physiological process corresponds to that observed following the removal of a kidney or partial thyroidectomy. Abnormally large and even small normal glands have been removed. The latter gave a strongly positive fuchsinophile reaction. The finding suggests that virilism may also be

associated with an apparently normal adrenal gland."

The most encouraging results have been obtained in cases of postpubertal virilism.

The author states that it is perhaps too early to speak of the ultimate value of the operations, and no hard and fast rules can as yet be laid down with regard to the selection of patients. In cases of prepubertal virilism, the results have been disappointing — "but this is to be expected, for an operation performed during the second decade is too late for a condition which manifests itself only at puberty and has been present for a considerable time" At present there is no method of determining adrenal dysfunction before puberty If this were possible, the results of earlier operation would be equally good. Time must of necessity be the final judge of a speculative surgical procedure A condition of slow or late development can be expected to regress slowly when only part of its cause has been removed

Psychologic Results — Psychologic changes do not occur in all cases of virilism but following operation changes in personality have occurred, such as homosexuality to normal sexuality

Summary—In over 60 cases of virilism, a family history of hirsutism was present in 25 per cent and appears to be transferred more on the female side. There is slight evidence that it is associated with events which occur at birth and it appeared in several persons whose mother suffered from exophthalmic goiter. In cases of mild virilism, there were symptoms of hyperthyroidism.

Most women with virilism are comparatively infertile and, if they conceive, they are apt to miscarry. One patient on whom adrenalectomy had been performed and who suffered from amenorrhea has since given birth to a son

"A series of 23 Broster concludes cases of virilism are presented in which unilateral adrenalectomy was performed without a fatality. We have found a specific differential staining reaction in the cells of the adrenal cortex, which is absent in controls. It is also present in the tumor cells in cases of virilism due to neoplasm This stain has been verified, and its presence shown in the opposite adrenal gland at autopsy by others This stain is present in the fetus of both sexes, and virilism can be explained by its abnormal persistence in the female In some of our patients we have observed an increased amount of cholesterol in the blood. We cannot say what the sigmificance of this stain is It is associated with definite changes in the growth and development of the body tissues, which have reverted to normal after unilateral adrenalectomy. In some cases it has been associated with alterations in the psychologic outlook of the patient, which have reverted to normal after operation."

TESTOSTERONE AND ANDROSTERONE

L. Stemach and H. Kun⁶ state. The normal urmary estrogenic substance content in six male patients was determined before the administration of testosterone or andiosterone propionate was begun. The general value was from 0 to 36 i upor liter, in one case 133 i u, was found.

The dose of testosterone propionate administered was 50 mg tuweekly and that of advosterone propionate 20 mg tri-weekly

Following the injection of 150 mg of testosterone propionate, *i.e.*, after the third injection, the excretion of estrogenic substance rose to between 67 and 100 r u , and in the case showing 133 i u before therapy, it rose to 416 r u. In the patient administered androsterone pro-

pionate, a corresponding rise was observed

The maximal rise occurred after 18 to 20 injections (900 to 1000 mg) of testosterone propionate. Treatment was concluded after 20 injections. The largest amount of estrogenic substance excreted was 1200 r u with testosterone proprionate, and 210 r u with androsterone benzoate per liter of morning urine.

They state the nature of the modified substance demonstrable in the urine remains doubtful, but the apparent possibilities are (1) estrone, estradiol, (2) substances of the male sex hormones with estrogenic effect, androstenediol (Butenandt), and (3) dihydroandrosterone (Dannebaum)

On discontinuing the injections, a sharp decline occurred, and in two to three weeks the pretherapeutic level was resumed

Stemach and his associate demonstrated that the follicular hormone produced well-developed hyperemia of the brain whereas the male hormones, androsterone, androstenediol, and testosterone, do not have this physiological effect upon the brain

Since the physiological testicular hormone contains the hyperemic factor, the injected artificial male hormone must be converted into this physiological form. In view of this, it appears possible to intensify the action of the artificial male hormone by combining it with a small dose of estrin. Early clinical results in hypertensive cases, as yet unreported, indicate the importance of combined therapy.

MENOPAUSE

Oestradiol Benzoate Therapy in Depression of Menopause — The authors, M S Jones, T N Mac-Gregor and H Tod,7 report their clinical studies of 17 cases in which the

onset of the depressive illness coincided with the onset of the menopause. "The psychiatric picture varies with each individual case, but all showed definite depression without retardation, agitation, partial or complete loss of interest in their surroundings, and insomnia, while in most of them suicidal ideas were expressed." In the majority of patients, biological assay of the urine for oestrin and gonadotropic hormones was made prior to the administration of therapy Five mg (50.000 ju) oestradiol benzoate were administered twice weekly, except during the menstrual period. The total amount of oestradiol benzoate given varied from 60 to 140 mg. Of the 17 patients treated, six made a satisfactory recovery, returning to their former occupations, and were well for at least three The period of hospitalization was reduced in these six patients to three months, the extreme being between two and five months, whereas an illness of this kind usually lasts at least nine months. Of the remaining 11 patients, five are still in the hospital, six have been discharged in an improved state The cases manifesting a less satisfactory response were among patients confined to the hospital for tour years prior to therapy and two cases in which a diagnosis of a paranoid state rather than a depressive state was possible in measurable quantities, was present in the name of four of the 13 cases tested. but only in very small amounts, in two of these cases, gonadotropic hormone quantitatively amounted to more than 50 mouse units (M L) per liter of nime, and in the other two it was less than 50 M. U. These four patients were all menstruating. Two others, whose urme contained no measurable quantity of oestrin, were also menstruating. These six cases in which menstruation was still going on all showed flushings and other indications of oestrin insufficiency

Of the 13 cases in which gonadotropic estimations were done before and after treatment, 11 gave at the start a gonadotropic finding of more than 50 M. U. per liter, and this was altered after treatment to less than 50 M U. In the remaining two cases, the results before and after treatment were both less than 50 M U In eight cases, the glucose tolerance curve after treatment was substantially lower than before treatment. This inhibition was found in all the cases in which In all cases, the patient recovered somatic symptoms, such as flushings and backache, which were present before treatment, were abolished by oestradiol benzoate

Summary—1 Seventeen cases of depression occurring at the menopause were treated with twice-weekly injections of 5 mg oestradiol benzoate. The total amount given varied from 60 to 140 mg.

- 2 Six of the patients made a good recovery within five months and have resumed their normal lives. The somatic symptoms were relieved in all the patients who had them
- 3 In 11 cases showing excessive amounts of gonadotropic hormone in the urine, oestradiol benzoate reduced the amount excreted

CHRONIC CYSTIC MASTITIS

Endocrine Therapy The authors' state that recent studies would seem to indicate that the breast changes in chronic cystic mastitis are associated with disturbances in some of the glands of internal secretion.

A frequent precursor of true cystic mastitis is cyclic pain in the upper and outer quadrant of the breast which reaches its maximum intensity before

the menstrual period The mammary pain and tenderness become more severe and eventually last throughout the entire cycle.

The patient with painful breasts is neither nervous nor underweight and in her thirties, she is either childless or has not been pregnant for a period of five or more years. Sterility is present in a high percentage of married women with this condition. Menstruation is usually regular.

The painful breast phase of chronic cystic mastitis may be successfully treated by endocrine therapy, intramuscular injections, twice weekly, of 10,000 i u of *estrogen* for a period of several months

Adenosis is characterized clinically by the presence of multiple indefinite nodules or small shotty masses in one or both breasts. In early cases the menses are regular and the breasts are usually of fair size with considerable parenchyma whereas, in fully developed adenosis, the menstruation is apt to be painful or irregular or the cycle is shortened to 26 days or less, the breast is diminished in size and the stroma is increased in density

The tender and dense areas of the upper quadrant, characteristic of the early painful phase, is present in adenosis

These patients are usually high strung, nervous, and underweight and often show a palpable thyroid and a definite adenoma is sometimes found

Estrogen is administered intramuscularly in 10,000 i u doses, from 50,000 to 120,000 i u are administered monthly for from two to ten months. In general, the therapy is highly successful, the pain is relieved and most of the nodules and areas of increased density disappear or are reduced in size. Recurrences may appear in a year or more after stopping therapy; however, the

recurrences are usually controlled by a single injection of 10,000 i. u. of oestrogen given at the premenstreum.

Cystic disease of the breasts is characterized by the development of one or more palpable cysts. It is most frequent in the nonparous women in the forties or near the menopause and in healthy women with regular menstrual cycles. Indurated areas and premenstrual pain in the breasts are unusual.

The cyst appears quickly in the breasts which are well developed but contains increased amounts of fatty and fibrous tissue. The cyst is freely movable, round and smooth, transilluminates clearly, and a cloudy milk-like fluid can be aspirated from it. A residual area of fibrosis remains where a cyst has spontaneously regressed. Multiple cysts may be present at the same time in the two breasts, however, this condition is a rare finding

The pathological changes of cystic disease are an increase in the amount of connective tissue, epithelial involution and hypermaturation and secretory activity in the surviving living cells of the terminal tubules

Oestrogen tends to inhibit the secretory activity associated with cyst formation and may complete the process of fibrosis. When oestrogen therapy is discontinued suddenly, continued unduly or administered in doses of over 20,000 i u weekly cysts may reappear. For this reason the results of oestrogen therapy in cystic disease are not as satisfactory as those obtained in painful breasts or adenosis.

In their opinion surgical excision of adenosis or cystic disease in the breast is unsatisfactory because the condition is chronic and nearly always bilateral and following excision, tends to appear in the same or opposite breast. Excision is required for microscopic examination when malignancy is suspected or

if the patient's apprehension concerning the benign nature of the breast pathology is inimical to her general state. One third of the cases studied showed multiple excision and amputation of one or more breasts. They believe that the mastectomy is not indicated

Relatively high dosage of oestrogen is required for successful results in chronic mastitis The plan of therapy used was 10,000 i u of oestrogen, injected intramuscularly, twice weekly for a period of three weeks (between two menstrual This is followed by weekly periods) injections of 10,000 i u of oestrogen during the second month and a similar injection every other week during the third month For the next three months. one dose of 10,000 i. u. of oestrogen is given in the premenstruum or oral capsules containing 2000 i u. of oestrogen are given every other day to complete the six-month period of therapy

Oestrogen is never given during menstruction

TESTOSTERONE AND EUNUCHISM®

A man, aged 38 years, had suffered a traumatic bilateral orchidectomy at age 19 years as the result of a shrapnel wound during the late war

In 1937 his apparent age was 24 to 28 his narrow shoulders, wide hips, feminine distribution of fat—at the breasts, abdomen and hips, the lack of masculine type of body hair, and the soft, non-muscular type of tissue, made his physique distinctly feminine. His voice was masculine, he shaved every other day, the phallus was of normal size but the prostate was small. Prior to the injury, he had strong libido and sexual function, but since the removal of testicles no erections had been possible. Desire was almost negligible.

Because of recurrent and cyclical attacks during the previous two years, of a facial and nasal eruption, with a coexisting conjunctivitis and eyelid edema, he was given daily injections of 20 mg of testosterone propionate The skin condition cleared up in six days under treatment with the previously used local skin application and testosterone proprionate whereas with local therapy alone it cleared up in two weeks. After eight daily injections he complained of persistent and painful priapism which was unrelieved by contus. Inquiry at this time revealed that he had been having nightly coitus and good orgasm was enjoyed but ejaculations had not occurred although the sensation had been experienced

Injections were continued twice weekly but the skin condition recurred and daily injections were resumed but this did not cause painful and persistent priapism. Normal erection and sexual function however continued

Therapy was maintained and four months later, at which time he was receiving 40 mg of testosterone weekly, libido was excellent, coitus took place twice weekly, intromission was easy, he had a pleasant erotic sensation but ejaculations had not occurred.

A mild increase in beard growth occurred and a few hairs appeared on his chest and he gained about 15 pounds in weight. Eight days after testosterone injections were discontinued erections became impossible.

In the discussion of the case the author calls attention to the case of Hamilton¹⁰ who administered about 40 mg of testosterone propionate three times weekly for a month and penile erections were noted after 60 hours. In both cases priapism, increased libido and improved mental and physical condition were observed.

Hamilton's case received a total of 550 mg. in 30 days and 940 mg was administered in 108 days in the present case. Normal sexual function was maintained by the injection of 40 mg a week but 20 mg a week appears to be inadequate, for erection was not spontaneous and cottus was only possible once a week.

The deductions made possible from therapeutic study are that 100 to 140 mg of testosterone propionate are required to restore sexual function and a maintenance of 20 to 40 mg per week is adequate

The author states that the dosage required for reversal of estrogen imbalance as suggested in the treatment of early prostatic hypertrophy would presumably be greater than these substitute doses. His (unpublished) experience in 20 cases of enlarged prostate with testosterone propionate indicate 50 mg daily for 14 days and then at increasing intervals. In these cases the power of crection was regained or increased only when large dosage was given daily

PSEUDO-CRYPTORCHIDISM AND TRUE CRYPTORCHIDISM

Differential Diagnosis Hamilton and Hubert ¹¹ because of the frequency with which spastic reaction" or physiological cryptorchidism occurs have devised a simple procedure whereby this temporary absence of the testes from the scrotum may be differentiated from true or anatomical cryptorchidism

A hot-water bottle that is filled with water at about 115° F (461° C) and covered with a single layer of flannel, is placed upon the scrotum—inguinal and permeum, the patient is then covered with blankets. After a half hour the muscles of this region are relaxed by

the applied heat, and if by this method the testes do not descend into the scrotum, even by increasing abdominal pressure, then digital palpation is employed. The authors warn against the use of cold hands and the stroking of the thigh during palpation of the inguinal region of the testes, as either or both will cause retractions of the testes from the scrotum. A well developed scrotal sac usually indicates that the case is one of intermittent retention.

Of the 16 cases referred to them as cryptorchid, they were able by this method to prove that 68 per cent of them were cases of spastic retention

Having drawn attention to a report of descent of a testis three hours subsequent to the injection of 100 r u of gonadotropic material, they later summarize "The high incidence of pseudocryptorchidism masquerading as true cryptorchidism leads one to question the large percentage of spontaneous descent in supposedly true cryptorchidism"

Further, it may partially explain, in various authors, the discrepancy in their results with endocrine preparations in the treatment of cryptorchidism

UNDESCENDED TESTES

Treatment With Anterior Pituitary-Like Substance¹²—The authors analyzed the published reports of 103 patients with 148 undescended testes. The condition was bilateral in 45 patients and unilateral in 59 patients. The successful results of anterior pituitary-like substance therapy was 83 per cent (25 of 29 cases) in the intraabdominal type, 61 per cent (22 of 35 cases) in the inguinal type, and 70 per cent (55 of 78 cases) in a group of cases in which the position of the undescended testes was unstated. Two

cases having an upper scrotal position responded 100 per cent to therapy.

In their opinion, the percentage of successful results in the intra-abdominal type may be somewhat too high, because of the lower percentage in the larger number of cases in which the location of the undescended testes was not stated

The migratory type of undescended testes, those which move back and forth from the canal to scrotum, has been demonstrated to remain permanently in the scrotum after puberty, and its variable position may lead to the recording of false results

In their study, 18 boys, from 1½ to 18 years of age, in which there were 21 undescended testes, 8 intra-abdominal and 13 inguinal, were administered 200 r u of follutein and A P L substance obtained from the urine of pregnant women—three times a week

Descent occurred in only 4 of 21 undescended testes in the 18 patients. In the four patients showing descent with treatment, the testis was in the inguinal canal, three of the four successful results were of the type that commonly descends at publish. Most of the 18 patients treated exhibited an increase in the size of the external genitalia and the findings at operation in several of the unsuccessful cases would suggest that anatomical factors were responsible for tailure of descent.

The patients received as large doses of A. P. L. substance as those of some authors reporting a much higher percentage of results. In their opinion adequate therapy was administered in the four successful results since descent occurred within one month. The external genitalia increased in size in all cases and the increase in size and vascularity of the genital organs appeared to make the subsequent operative procedure less difficult. They consider it advisable there-

fore, to treat all cases of undescended testis with injections of A.P.L. substance from four to six months and to carry out operative procedures in those in whom descent fails to occur

 $D_T/\Lambda/D$ Bevan expressed the following opinion of the therapeutic study

"One of us desires to express separately the following opinions concerning the value of the anterior pituitary-like principle in the treatment of undescended The research is as yet in the experimental stage. There is evidence that this principle is a growth stimulant to the male genitals. The reports in the literature of its powers of producing rapid descent in a large percentage of cases appear to be exaggerated. Further experiments with this agent in a large series of cases by men who are thoroughly familiar with the anatomy, the embryology, the clinical history and course, and the operative treatment, should be made in order to determine scientifically its value, if any. There is as yet an uncertainty as to the risks and the value of bringing on changes which simulate an artificial puberty in a child of seven or eight years. In our series I have not seen any evidence of injury and teel that we are warranted in continuing the use of this as an experiment use is followed by descent well and good If after SIX months trial no change occurs, the child should be given the benefit of an operation with the purpose of bringing the testis into the scrotum before the advent of puberty

CRISES IN SEVERE HYPERTHYROIDISM

Lahev¹, believes acute crises in patients with severe hyperthyroidism are brought about by tactors quite remote from the thyroid, and that the acute state is caused by, and persists because

of, the secondary effects of hyperthyroidism on liver function.

He has believed that when acute thyroid crises eventuate, some other factors have become involved, as indicated by the frequent and quite sudden occurrences at this time of a different group of symptoms, viz, delirium, vomiting, diarrhea, and temperatures to 105° to 106° F (40.5° to 41 1° C.). From a clinical standpoint, this suggested liver effects, because of the beneficial effect obtained from intravenous administration of glucose and fluids and the low normal glycogen content of the liver in patients dving of severe hyperthyroidism This also serves to explain the high febrile reactions

As the result of this clinical experience, the combative measures in the control of hyperthyroidism include not only rest and jodine and sedatives, but also protection of the liver by the continuous administration of glucose Subtotal thyroidectomy is recommended in all patients with hyperthyroidism who show no progression or improvement after three or four weeks of nonoperative treatment, those who exhibit mild cardiac failure or cardiac arrhythmia should be immediately prepared and operated upon without preliminary trial of non-Auricular fibrillaoperative measures tion with hyperthyroidism, particularly because of the frequent deaths due to emboli in this condition, should be accepted as an indication for immediate surgical measures — the same position holds true for diabetes or pregnancy associated with hyperthyroidism

A progressively rising pulse rate and continued loss of weight indicate that hyperthroidism is increasing. Infections with high temperature intensify the existing thyrotoxicosis, and in a mild case of hyperthyroidism, may precipitate thyroid crises. A change in the psychic

state or the appearance of vomiting or diarrhea, indicates the possibility of the onset of a serious thyroid state.

Glucose therapy continuous intravenous administration of five per cent glucose—40 to 60 drops per minute, together with the frequent administration of 50 per cent glucose intravenously, so that the patient receives from 500 to 800 grams of glucose in 24 hours. In cases with vomiting or delirium, 50 drops of Lugol's solution is added to 1000 cc of the fluid introduced intravenously

Lahey believes that these patients, having been relieved of their immediate danger by the checking of the diarrhea and vomiting, should be placed on a high carbohydrate diet for two or three weeks and then operated upon by the stage method—right subtotal thyroidectomy, and at the end of six weeks, left subtotal thyroidectomy, thus permanently insuring them against a recurrence of their critical state by completely relieving them of their hyperthyroidism

HYPOTHYROIDISM

Cretinism and Myxedema—Gardiner-Hill¹⁴ states that sporadic cretinism bears little resemblance to endemic cretinism, and is found in regions where goiter is not endemic

Heredity is seldom a factor in producing the picture typical of simple athyroidism, but thyroid maldevelopment and, more frequently, acute thyroiditis, caused by an infective disease in the mother during pregnancy and resulting in atrophic changes in the fetal thyroid—are the likely causes

The clinical features of cretinism are disproportionate dwarfism, mental retardation, and delay in sexual development. The limb measurements are unduly short when compared with the trunk, and osseous development is re-

tarded—delayed appearance of centers of ossification and growth of the long bones. The mental retardation varies; reactions to stimuli are slow; and in the untreated case, imbecility results. Puberty may be indefinitely delayed.

Diagnosis—The characteristic facies, the pasty and sallow complexion, the large broad thick tongue, the dry hair, and the subnormal temperature, together with the aforementioned features, distinguish cretinism. In its less characteristic phase, roentgenograms of the wrist will show the delay in the ossification. In older children the B. M. R. can be determined, and will be found at a low level—40 to 50 minus.

Myxedema in adults has similar clinical features of cretinism except there cannot be the associated growth disturbance and there are regressive changes in the genital organs. Myxedema is insidious in its onset and presents itself under various guises

Mental changes are frequently the earliest symptoms and it is not at all uncommon for the patient to be unaware of any deterioration in health.

The statistics of 101 cases of myx-edema observed by Gardiner-Hill showed that in 50, the diagnosis was made during treatment of some intercurrent illness and in the remaining 51, 19 complained of general swelling of the body, face, hands and feet, 17 observed loss of power and sensory disturbances, i.e., pins and needles and numbness of the limbs, and 18 mentioned as one their first symptoms, lethargy, weakness, and undue fatigue. Other symptoms were menorrhagia and floodings, voice and speech changes, loss of memory and loss of hair.

Some patients sought medical advice because of obesity, sterility, miscarriage and still births or chronic rheumatism Myxedema, because of its various guises

and its symptoms indicative of local disease, finds the patients seeking treatment in gynecological or other special departments.

Treatment—The results of treatment of cretinism and myxedeina are on the whole satisfactory. Most cases of cretinism and myxedema are extremely sensitive to thyroid extract, so it is best to begin with a small daily dose and gradually increase it until, at weekly intervals, the appropriate maintenance dosage is determined. The problem of dosage is almost identical in childhood and in adult myxedema.

The usual method is to begin therapy with ½ grain (16 mgm) of thyroid once a day for seven days, then ¼ grain (16 mgm) twice a day for another week, then ½ grain (32 mgm) twice a day for the third week, after which the dose is increased until ½ to 2 grains (97 to 129 mgm) are being administered daily—the usual maintenance dosage for myxedema

Overdosage of Thyroid Extract—Overdosage and thyrotoxemia are distinct entities. The effects of overdosage disappear quickly on stopping therapy, the effects of thyrotoxemia are more lasting, and are most likely to occur when thyroid extract is administered during an infective illness, such as, influenza or tonsillitis.

Patients requiring maintenance dosage should stop therapy for three to four days a month, in cases of overdosage, therapy should be discontinued one to two weeks, then resumed at half the dosage, providing the untoward symptoms of tachycardia, undue nervousness and excessive weight loss, have disappeared

The thyroid preparations used consist either of the fresh gland or of desiccated, or dried gland extracts. The latter are five times stronger than the fresh gland, are more reliable and more stable,

as well as being superior to synthetic thyroxin

IODINE IN ADENOMATOUS GOITER

Jackson and Freeman15 report their study of a series of 279 typical toxic adenoma cases in which operation was They find that the basal performed metabolic rate is the most tangible factor available for estimating the degree If all cases are of thyrotoxicosis considered, they might conclude that aqueous solution of iodine does have a beneficial effect, because the average metabolic rate in the whole series was found to be decreased following iodine Further analysis of iodine administration in the cases, however, revealed that approximately 62 per cent were benefited or were not affected, and in approximately 38 per cent of the cases the basal metabolic rate, the tremor, tachycardia and the like were definitely made worse by jodine. These later deductions are in agreement with those of Goetsch but differ from those of Means and Lerman and are in marked contrast to those of Youmans and Kampmeier, who report that the response to jodine treatment in 30 unselected patients with toxic adenoma, who were previously untreated with iodine, was essentially the same as that seen in unselected cases of exophthalmic goiter

The authors summarize the study in the following manner

- 1 There may be produced iodine tast cases of exophthalmic goiter
- 2 Iodine not only does no good but is definitely contraindicated in nontoxic adenomas of the thyroid
- 3 There is danger, in administering iodine in cases of adenomatous goiter, of producing "iodine hyperthyroidism"
- 4 Adenomatous goster does not become toxic before the patient has reached

the age of 30 unless the toxicity is brought on by the injudicious use of iodine

- 5 We have shown that iodine may and does produce thyrotoxicosis in adenomatous goiter as opposed to the contention of Mean and Lerman
- 6 The effect of aqueous solution of iodine in toxic adenoma is not constant or specific and is not the same as that produced in exophthalmic goiter
- 7 Approximately 62 per cent of all cases of toxic adenoma are benefited by iodine or are not affected, while 38 per cent are made worse
- 8 In a series of cases of toxic adenomas, toxic symptoms and the basal metabolic rate were aggravated by aqueous solution of iodine
- 9 Owing to its variability of action, we believe that iodine should be given as a routine in all cases of toxic adenoma before and after operation, because two thirds of the cases will be improved, and the harmful effect on the other third is negligible over a short time

Conclusions—1 Iodine should not be given to patients with nontoxic thyroid adenomas

- 2 The condition termed iodine hyperthyroidism is a definite clinical entity
- 3 Aqueous solution of rodine has an moonstant effect in toxic adenomas

HYPERTHYROIDISM IN CHILDREN

(r E Beilby and J C McClintock¹⁶ state exophthalmic goiter presents the same basic symptoms regardless of the age at which it appears. However, greater emotional instability and the growth stimulus brings about a more rapid progress of the disease in children. Hyperthyroidism in children under five years of age is rare, however, adolescent enlargement of the thyroid gland, especiation.

cially in girls, may present mild symptoms of hyperthyroidism. In their opinion it is far more dangerous to attempt to cure hyperthyroidism in the young by medical means than it is in the adult As a result, in the increased metabolism associated with hyperthyroidism. skeletal growth advances beyond the age in years. The hyperthyroid child becomes thin, the weight may remain stationary or be reduced in spite of increased food intake. The symptoms of hyperthyroidism in children and the frequency of the same, as determined from the report of three authors, were tachycardia, nervousness and thyroid enlargement in over 90 per cent, weight loss, weakness, exophthalmus in over 60 per cent Bruit, tremor, gastrointestinal disturbances about 50 per cent, and polyphagia in 40 per cent

The trequency of the occurrence of this disease increases as the age of puberty approaches, with the female being more commonly affected than the male, with a ratio of about four to one

In their series of over 3000 patients with all types of goiter the authors observed only eight instances of the disease, all in girls, and before the onset of the menstrual cooch. The ages of these patients were 214 years, 41; years, 9 years, 11 years, 13 years and three cases at 12 years of age. True hyperthyroidism must be differentiated from that group or patients who are diagnosed - functional neurotic" or the nervous type of girl who is tall and thin Although these latter patients have an increased pulse rate and an increased trulse pressure the pulse rate is variable and fluctuates over a wide range returns to normal at the bed rest and during sleep, whereas, the pulse in exophthalmic goiter is high even during skep. Other differential diagnostic features of functional neurosis from true

hyperthyroidism are lack of retraction of the upper lid, moist cold hands and the anorexia. The thyroid gland may be slightly enlarged but has a soft pulpy feeling as contrasted with the meaty firmness of exophthalmic goiter.

Other diseases concerned in the differential diagnosis are tuberculosis, chorea. and rheumatic heart disease. In their opinion it is almost impossible to obtain an accurate basal metabolic test in children and reliance on the basal metabolic rate as a diagnostic feature of hyperthyroidism is more dangerous than in the adult. Iodine is of value only as a therapeutic diagnostic aid and as part of the preoperative management of the patient. Once the diagnosis of exophthalmic goiter is established, it is imperative that the child have an opportunity to benefit from surgical treatment since no other method obtains as satisfactory results nor has such a low mortality They concur in the opinion of Albert that it is difficult to be too radical in the removal of thyroid gland in children because of its inherent tendency to hypertrophy, and their experience of recurrence in one of the cases reported confirm their earlier opinion, which states that it is necessary to remove slightly more tissue from the thyroid gland from the young patient than is the custom in the adult patient. This is, they note, not in agreement with most of the opinions expressed in the literature today

I wo cases of hyperthyroidism are reported, which present pertinent factors relating to the subject. Case one of the report concerns a child of age eight years who was operated upon at the age of 234 years because of typical exophthalmus goiter. One year after operation, return of the symptoms and goiter necessitated a second operation. Since this time she has remained well and has

presented no symptoms suggesting recurrence of hyperthyroidism. The exophthalmus present at her first admission has improved, however, unequally, the right eye is more prominent than the left. The history of the patient indicates that the onset of the disease occurred before the age of one year. X-ray study of the wrist, at age four years, revealed an osseous development corresponding to that of a nine-year-old child. Three years later, osseous development corresponded with that of a 12-year-old child.

Case 2 is that of a female child of age 413 years The chief symptoms were nervousness, sudden loss of weight, irritability, and weakness Physical exammation showed a tall thin girl, lying restless in her bed Exophthalmus and lid lag were present. Thyroid gland was diffusely enlarged, the extended fingers and protruded tongue showed a fine tremor Basal metabolic rate, based on weight, by the Benedict-Talbot method, showed 1222 per cent. The rate based on height, after the Benedict method, was plus 875 per cent. X-ray examination of the skeletal system showed normal development. The pulse rate on admission was 140 and after rest in bed varied between 110 and 130 stage operation was performed, the pulse rate rose to 200 after the first lobectomy and the temperature rose to 103° F A less marked pulse and temperature reaction occurred after the second lobectomy The pulse later subsided to between 80 and 100, and the temperature became normal

THYROID EXTRACTS IN CONDITIONS OTHER THAN MYXEDEMA

Lyon¹⁷ suggests The use of thyroid extract in mild degrees of *subthyroidism* characterized by one or more of the fol-

lowing symptoms — dry skin and hair, mental depression or dullness, forgetfulness, loss of energy, tendency to chronic constipation, predisposition to colds, and some vasomotor disturbances. A usual confirmatory sign is a thinning or loss of hair from the outer third of the eyebrow. In this class of patient the improvement under thyroid therapy is often remarkable.

Thyroid extract in *obesity* is often unsuccessful, for it increases the appetite. The B M R in obesity, unless it be of hypothyroid origin, is not abnormal since it is calculated on the area of body surface, and because of the obese individual's increased surface, the metabolism may actually be in excess of that of a person of average proportions

The plan recommended in the treatment of obesity is, first, to reduce weight by a 1000 calorie diet, and when the weight reduction becomes stationary to introduce thyroid extract as an adjunct, the dosage of which is increased gradually until satisfactory weight loss is being obtained on the combined treatment. When reduction of weight has been completed, a few patients can keep their weight down without further treatment, some require a restricted diet, and others require a small dose of thyroid extract to maintain the reduced level of weight

Thy roid extract is of some value in the treatment of *asthma* when the breathing is embarrassed by the excessive fatty covering of the chest. In lean individuals its use must be restricted, since an increase in metabolism is undesirable

Thyroid extract in *dermatology* It is mostly advised in chronic conditions of a noninflammatory nature, chiefly *ichthyosis* In psoriasis, evidence of its beneficial effect is not clear.

Thyroid extract in the chronic edemas of renal disease. It may be of definite

assistance in the *nephrotic syndrome*, since diuresis is commonly observed in myxedema and other cases under thyroid therapy.

Thyroid extract is indicated when subthyroidsm develops in a case of goiter. It has been advised in cases where potassium iodide is used, i.e., arteriosclerosis, fibrositis and chronic rheumatism, probably with the idea of stimulating local metabolic changes and increasing the removal of waste substances.

ENDOCRINE DWARFISM

Schaefer¹⁸ reports the end results in 11 cases of endocrine dwarfism treated with an experimental growth extract obtained from the *anterior lobe of the pituitary*. The period of therapy in a (previously reported) group of four cases was $2\frac{3}{4}$ years and in the new group of seven cases was from 6 to 19 months (Therapy was discontinued in one case because of completion of sexual maturity and closure of the epiphyses)

Chondroepiphyseal changes were observed in two patients. The changes observed were such as the moth-eaten, fuzzy, ragged and poorly outlined appearance of the osseous centers together with decreased bone density.

Results—In the four patients receiving therapy for 23 years, the average actual growth increment was 71 inches, exceeding by 31 inches the estimated average normal growth of 4 inches

The second group of seven patients showed an actual growth over the average period of treatment—117 months of 22 inches as compared to a corresponding normal increment of 19 inches

The growth increment of the two groups of patients were determined for the periods preceding therapy. The factors used in the determination were the histories, former measurements and the

actual heights at the time therapy was started. The assumed growth curve of the cases, for the period corresponding to the duration of therapy, was estimated at 19 inches in the first group and 0.5 inches in the second group

A tolerant dose of the thyroid extract was administered as an adjunct to the growth hormone therapy. The author believes this is a valuable adjunct in treating pituitary dwarfism whether or not hypothyroid findings are demonstrated.

The dosage of the growth fraction was two or five cc twice weekly; the latter dose was used in the later months of the period of therapy in the first and second group, and in a few cases in the latter group throughout the period of therapy.

The summary states that statural height in excess of normal growth for their individual ages and periods of treatment has been induced. The pituitary dwarf is a proportionate individual (A comprehensive diagnostic survey should be made to rule out nonendocrine cases of dwarfism before therapy is instituted.) Pituitary dwarfism has been associated with generalized chondroepiphyseal changes, such as Osgood-Schlatter's, Perthe's and Kohler's disease

It had been previously noted that the extract was capable of producing amenorrhea in two patients with normal rhythmic menstrual periods, and in an adult male aged 32 years destroying libido entirely during the course of treatment.

He concludes that the pituitary extract (Antuitrin G) was the responsible factor in the production of growth in these dwarfed human beings. Thyroid extract has proven clinically and experimentally a valuable adjunct in treating pituitary dwarfism. Roentgeno-

graphically—a delay in osseous development is a good prognostic sign. Contramidications for the administration of the extract are epiphyseal closure and approaching sexual maturity.

Note-The findings of Dr Schaefer are important because the two anterior pituitary extracts used differ in composition. In the later series of cases, the extract used showed, experimentally, increased animal potency as well as purification and elimination of other intrinsic Some of the early pituitary factors cases exhibited a rise in B M R under Thyrotropic factor was not bioassaved in this preparation. He states that the results obtained, while not conclusive because of the short period of clinical observation, indicate that the purified extracts exhibited no enhancement of the earlier results but 'this proposes the questions as to whether an admixture of these various pituitary hormones might not prove to be the therapeutic epitome in human dwarfism"

This study clearly defines the difficulty which confronts the physician who seeks to apply the results obtained by others in endocrine disorders

This study cannot be considered a true clinical test of growth fraction of the anterior pituitary lobe therapy because tolerant doses of thyroid extract were used in conjunction with the injections of the growth fraction. Thyroid extract per se has growth stimulative properties and in order to clinically evaluate a growth hormone preparation, it must be exclusively administered.

In a larger series than here reported, the writer has administered growth hormone, however, in 50 per cent smaller dosage, without observing an increased growth increment. On the contrary, our only growth effect has been observed with the oral administration of *unpurified anterior lobe extract*, 1 to 3 grains

daily, depending upon the age of the case, and in conjunction with low dosage of thyroid extract— $\frac{1}{10}$ to $\frac{1}{3}$ grain (6 to 21 mgm), depending upon the degree of obesity. Cases which had failed to respond after one year of growth hormone therapy have responded to the combined oral therapy and in a striking manner, as much as three inches a year for a period of six years

CUSHING'S SYNDROME

In the study of pituitary disorders, the greatest progress has been made in our knowledge of "Cushing's syndrome" or pituitary basophilism, first described by Cushing in 1932, at which time it was thought caused by an adenoma of the basophile cells and a secondary adrenal cortical hyperplasia or adenoma. This disturbance was found chiefly in young white temale adults. However, it has since been observed in a young female mulatto.

It is now known that the Cushing syndrome is produced by endocrine glandular pathology other than a primary basophilic adenoma of the anterior pituitary lobe of the pituitary gland Carcinoma of the anterior pituitary lobe and anterior pituitary chromophobe adenoma, or adicual contical carcinoma, arrhenoblastoma of the ovary, caremoma of the thymus, are all able to produce Cushing's syndrome. So far, the only determined pathological factor common to all is the hyaline change in the pituitary basophile cells-known as the "Crooke reaction"-which causes the characteristic clinical picture, viz, regional plethora, rapidly gained regional obesity, kyphosis, hypertension, hypertrichosis, genital dysciasia, purplish striae, debility, and osteoporosis

It is therefore evident that there exists a benign and malignant etiology in the

Cushing syndrome, so therapy will be dependent upon this differentiation

In a case presenting the aforementioned clinical picture, the x-ray exammation is, of course, extremely helpful in the clinical survey. If the sella turcica is enlarged, the indication is strong that it is a pituitary lesion, however, a basophilic adenoma of microscopic size can cause the syndrome, in which event the sella will not be enlarged. The finding of osteoporosis, usually localized in the skull, ribs or vertebrae, is very signifieant. As adrenal lesions are next in incidence, x-ray investigation of the adrenal regions is also advisable obtain a more precise definition of the adrenal gland, injection of air into the periadrenal tissue is used in some clinics, with very promising results. Another method is to define the kidney shadow with an opaque agent, and so observe any distortion of normal shadow. These procedures may be combined to advantage. If both pituitary and adrenal regions are normal x-ray of the mediastinum is advised to eliminate a thymic I sion

In every amenorrheic female in whom the clinical picture suggests the Cushing syndrome a vaginal examination should be made, because the physical contour is frequently that of a pregnant woman, and since amenorphea is an almost constant sign the two conditions are strikingly similar physically. In the suspected male case, a semen examination is advisable

Recently I observed a case in whom a regative I riedinan test was reported, and who had clinically responded to intensive and continuous progynon B and proluton therapy during the past three years. Her last menses was July, 1936, the briedinan test was negative in March 1937, physical and x-ray examination of July, 1937, showed a six months fetus, and on October 25, 1937,

she gave birth to a male infant. The infant was very hypertrichotic, but otherwise normal

The adrenogenital syndrome may in some instances simulate the Cushing syndrome, and if x-ray and clinical investigation fail to define the glandular pathology, an exploratory operation of the adrenal and ovaries may be required

The classical Cushing's syndrome is generally fatal in five years after onset. Few authors have ventured to define what might be termed the early manifestations of the disorder. In the writer's opinion, the early phase, in a patient who also exhibits psychic depressive changes accompanied by unexplained weakness, consists of regression of gonadal function, increase in the pilous system and systolic blood pressure, and sudden regional weight gain. Associated with this are the various skin changes, as coarsening of the skin, acne and reddish or purplish striae.

Therapy — The therapy of Cushing syndrome is chiefly x-ray treatment of the pituitary gland. This form of treatment was first used by Cushing J. F. Bromley 19 reports the results of x-ray therapy in seven cases of baso-The following philic hyperpituitarism technic was used 200 KV constant potential, filters 1.5 mm of copper + 0.5 mm of aluminum, 40 cm tocus skin distance, fields 6 by 8 cm, 1500 to 2200 r u administered in two to ten weeks the course of treatment being repeated when necessary. It is stated that results were satisfactory in most cases and proved beyond doubt that x-ray treatment is worth trying in cases presenting sexual dystrophy, hypertrichosis regional obesity and hypertension P B Bland and L Goldstein²⁰ reported a successful result in one case of Cushing syndrome. Our personal experience in two cases who received

two series of x-ray treatments was disappointing

During the past three years a corresponding group of 11 cases have been treated with from 25,000 to 50,000 i u of progynon B injections and supplemental doses of 1 to 2 i u proluton. The progynon B injections are administered two or three times weekly until marked improvement occurs in the physical appearance and symptoms

After the symptoms are relieved, an attempt is then made to induce or improve the menses, by administering a series of proluton injections 2 to 5 i u every day for four or five days

It menstruation does not occur seven to ten days after the last injection of proluton, a new series of progynon B injections is given. The dosage of progynon B may then be started at 10,000 i u every third day for the first ten days and during the second ten-day period from 25,000 to 50,000 i u, three or four days after the last dose of progynon B is administered another series of proluton is given to induce menses.

A recurrence of one or more acute symptoms such as severe headache or migrame irritability, depression, cardiac anxiety or a rise in systolic pressure requires the administration of an additional dose of 25,000 to 50,000 r u progynon B, irrespective of the routine schedules of therapy. The reappearance of acute symptoms usually occur at or about the time menses should occur

The therapy is maintained for months or until clinical improvement warrants stopping therapy or diminishing dosage and or frequency of administration

PITUITARY INFANTILISM WITH DIABETES

Sexton and Neuhoff²¹ state that three conditions appear to contraindicate the

use of anterior pituitary extracts in cases of pituitary infantilism with diabetes

- 1 The diabetogenic substance present in the anterior lobe
- 2 The high incidence of hyperglycemia and glycosuria in acromegaly, and
- 3 Evidence tends to show the presence of the diabetogenic substance in growth extracts

The case reported is a woman aged 25 years who complained of a weight loss of 20 pounds during the previous ten months, retarded statural development, primary amenorrhea, absence of secondary sex characteristics, weakness, nervousness, fatigue, constipation and painful and involuntary urination on occasions when excited

Her height is 56 inches, her body measurements are proportionate, and the weight is 68 pounds. Her facial appearance depicted her true age, in contrast to her well formed, immature body. She lacked both primary and secondary sexual development. The blood pressure was systolic 96 and diastolic 66 mm of Hg. Her temperature was 98.2°

Utine analysis showed. Specific gravity 1028, sugar four plus, aceton two plus and diacetic acid was present

The authors state that insofar as could be determined from the history, the diabetes developed at age 19 years. The case is paradoxical in that hypopituitarism is commonly associated with augmented sugar tolerance. Sexton found a low normal fasting blood sugar to be the rule in pituitary dwarfism.

Note — In collaboration with Di Joseph T Beardwood, Ji, a limited number of children and a girl of 18 years having evidence of pituitary dwarfism or retarded growth development and diabetes have been administered **Collip's Growth Factor**, one cc three times a week. We have observed no deleterious

physical effect or disturbance in their diabetic standardization resulting from growth hormone therapy. No evidence of increased growth effect has to date followed the administration of the growth fraction.

HYPERPITUITARISM

Levy-Simpson²² states, "Acromegaly is the result of excessive secretion of the growth hormone from an unusually enlarged pituitary and its contained eosinophil adenoma"

In a case where an eosinophil adenoma is absent, a cell count will reveal a relative excess of the eosinophil cells or a developmental pituitary rest and of eosinophil cells in the sphenoidal air sinuses

The enlarged pituitary gland may press on the optic chiasma, and may erode its walls and invade the brain or the cavernous sinus

The clinical manifestations usually have an insidious onset, therefore the disease may be in progress for several years before its characteristic features are observed by the patient, leading him to seek medical advice. If the disease has its onset in childhood or adolescence while the epiphyses are united, giantism occurs, and if the hypersecretion of growth hormone continues, aeromegaly is superimposed on the pre-existing giantism. If the onset occurs in adult life, the epiphyses are united so only aeromegaly result.

The skeletal changes are prominent becept for occasional periosteal thickening the long bones usually escape the pathological process of enlargement, characterized roentgenographically by the tutting of the phalanges. The hands and feet enlarge, due in part to the thickening of the soft tissue. The fingers are usually short and spade-like, unless the

onset was in early life, in which case they may be long and tapering. The skull is considerably thickened, especially the ridges and external occipital protuberances, which become prominent. The enlargement of the facial bones is prominent and diagnostic. The malar bones and the zygomatic arches are thickened and enlarged (superior maxillary prognathism) and the lower maxilla enlarges and protrudes forward (prognathism)—the overgrowth causing separation of the teeth. The diameters of the thoracic cage are increased, and the vertebrae may undergo atrophy, hypertrophy and partial fusion, with resulting kyphosis, lordosis and scoliosis. The insertion of the muscles or tendons become prominent and exostoses occur near joints and the thickening process may involve the joints, with resulting arthritis

There is early muscular hypertrophy and attendant abnormal strength that is eventually succeeded by muscular atrophy, atony and weakness. The thickening of muscular tissues, soft organ tissue, is generalized, and this results in enlarged tongue and hips, broad thickened nose, enlarged pores, hypertrophicd sebaceous and sudoriferous glands, increased hair growth, enlarged larving with its deep resonant voice, and enlarged air sinuses.

The cardiovascular system reveals an enlarged heart, hypertrophy of the coats of the peripheral blood vessels varieose vems are common. Hypertension occurs, which in the late stage of collapse is frequently followed by hypotension, and acroevanosis and Raynaud's phenomena may result.

Neurological maintestations are: impaired smell due to hypertrophy of the turbinates, optic atrophy, bitemporal hemianopia, and later, complete blindness of one or both eyes—due to the pressure on the optic chiasma, ocular

palsies from third, fourth and sixth nerves' pressure, and involvement of the fifth may produce pain and hyperesthesia of one or more of its branches. True neuritis occurs when the somatic nerves are caught in the obliterated intervertebral foramina. Various types of chronic inflammation of the meninges of the skull and spinal cord are described. Areas of sclerosis in the cord may occur, and result in ataxia and pseudotabes.

Memory is often impaired, and depression, irritability, melancholia mania and delusional insanity may occur

Speech is sluggish and slow, with apathy and lack of initiative demonstrated by part of the general behavior

Headache, of bursting character, may be severe, while quite intractible to medical therapy, the headache may be temporarily relieved by removal of the 30 cc. spinal fluid which is usually under considerable pressure.

In the early phase especially in adolescence, there may be an increase in libido sexualis, more frequently there occurs amenorrhea and impotence. In other cases no change in sexual function is observed for years after the onset of the skeletal, and tissue changes consequently, normal mensionation pregnancy and partition take place in acronicially

The diabetogenic factor of the anterior lobe is an important, it not sole, factor in the production of the glycosuna which occurs in 50 per cent of acronegalics, as well as the diminished sugar tolerance. The disturbance of carbohydrate metabolism results in boils, cataracts, and coma. The severity of the diabetes reflects the severity of the acronegaly, similarly, when the hypopituitary state succeeds the hyperpituitarism, a low blood sugar and increased tolerance occurs. Both atrophy and hypertrophy of the pancreas and the islands of Langerhans have been noted.

Despite the fact that in 50 per cent of acromegalics, the thyroid is somewhat enlarged, hyperthyroidism is comparatively rare, but exophthalmus is not uncommon.

The course of the disease varies from a long chronic progressive state that may have waves of remission and progression towards a stationary phase lasting some years, to a type that will incapacitate in a few years

The mortality is ten per cent, and improvement occurs in about 70 per cent of the cases

Therapy—If the optic nerves or the cranial nerves are involved, surgical removal of the pituitary tumor is indicated. In other cases, x-ray therapy is indicated, which will result in improvement in 50 per cent of the cases

Note—X-ray and surgery continue to hold therapeutic value in the treatment of acromegaly. X-ray is usually conceded to be the elected method of therapy, if the signs of the optic nerve or chiasmal pressure are absent or minimal. If, in spite of x-ray therapy, the ever findings show progression of the pressure on the optic nerve or chiasma, surgery is then considered to be the elective therapy, in order to preserve vision.

Kirklin and Wilder²³ observed marked improvement in cases of acromegaly from the administration of *estrin* substances, 1000 i ii were given daily, or every other day for many months to a year. This therapy attempts to inhibit the anterior pituitary lobe function. It was found to be of value only in those who were in the fourth decade of life. The younger individuals failed to respond.

Zondek has produced experimentally a pronounced degree of pituitary inhibition, but he has observed that the tropic factors of the anterior pituitary lobe are not simultaneously inhibited Treatment of Pituitary Tumors—Biggart and Dott²⁴ report the indication for *surgical intervention* in cases of pituitary tumor is usually a progressive impairment of vision from compression of the optic fibers at the chiasma optic nerve or tracts. Surgery is rarely resorted to in an attempt to combat endocrine disturbances. In a few cases of rapidly progressive acromegaly, which may become serious, surgical removal of the adenoma is probably justified in an attempt to arrest its progress.

The place of radiotherapy in the management of pituitary tumors is, in their opinion, at present undetermined Improved technic gives promise of better results, radiotherapy has no obvious effect on tumors other than the adenoma Radiotherapy is used regularly as a sequel and adjunct to subtotal surgical removal and in the primary treatment of adenomas in which visual impairment is absent or very slight. Results in the past year suggest that this treatment may suffice

Levy-Simpson Syndrome — Giantism or excessive height may be due to hypersecretion of growth hormone betore the epiphyses tuse or to delayed union of the epiphysis which permits the growth hormone to continue its effect for an abnormally long time, or to a combination of the above factors

The pituitary gland in this condition may appear normal or enlarged and histologically it may show a normal picture or a selective increase of, or adenoma of eosmophil cells

The excessive growth is generally observed in childhood or may be more noted in adolescence. Acromogalic features occur in about 40 per cent of grants, and is observed at puberty, in adolescence, or in adult life.

In the pituitary eunuchoidism the external genitals are small and the second-

ary sex features are deficient or absent The hypogonadism results in ununited epiphyses, and the growth hormone is effective in continuing growth. This type of growth is disproportionate, and is extremity growth.

In other cases sexual development and its attendent secondary features may be normal or excessive at first, but later, impotence may occur

Note—The therapy of giantism presents a most difficult and intricate problem. In cases of eunuchoidism it is patent that gonadal stimulation is required to close or unite the epiphyses and stop vertical growth. The difficulty here arises in obtaining a pituitary gonadotropic preparation in adequate dosage that is free of growth hormone. To date we know of no such preparation which has had sufficient clinical trial to advocate its usage.

FRÖHLICH'S SYNDROME

The Frohlich syndrome continues to be debated etiologically as to whether it is a pituitary disorder, or whether it is a hypothalmic lesion. The close proximity of both structures makes it most difficult to decide, yet its etiological determination will facilitate therapy for the condition. The prevailing thought is to ascribe the condition to an anterior pituitary disorder.

Su Walter Langdon-Brown²⁵ believes that many cases labelled Frohlich's syndrome are really instances of a temporary pre-pubertal obesity due to functional delay in the development of the pituitary

Diagnosis—Diagnosis of the Frohlich syndrome or adiposogenital dystrophy is made by the peculiar teminine body figuration, the characteristic fat deposits in the manimary and limb girdles, the lack of genital development

and secondary sex characteristics, and the mildly dull mental and physical state.

The skin of the face is usually of the peaches and cream complexion, and is generally of soft thin texture, and bruises easily According to Sir Langdon-Brown, the male external genitals are underdeveloped and the testes may be cryptorchidistic, in the female there is amenorrhea and infantile uterus, and the breast parenchyma is diminished.

Therapy—The treatment advised is a 1000 calorie *diet* whose carbohydrate content is obtained from five per cent vegetables. As it is known that a sense of exhaustion frequently occurs in reduced dietary intake in cases of obesity, the taking of small amounts of *dextrose* overcomes this state which is the result of low blood sugar

The endocrine therapy recommended is —early small dosage, $\frac{1}{10}$ grain (6 mgm) of thyroid twice daily, which is gradually increased, and alternately 2 to 5 grains (129 to 324 mgm) of anterior pituitary extracts may be prescribed with each dose of thyroid

Children under 12 years of age should be given a proportionately smaller dose of thyroid

UNUSUAL PITUITARY SYNDROME

The authors of an article in the Quarterly of Medicine Journal²⁰ describe six cases exhibiting anterior pituitary and gonadal insufficiency which presents possible direct or indirect relationship with a blood dyserasia because of the associated anemia—achlorhydria and subacute combined degeneration of the spinal cord

The syndrome occurred in four men and two women, the range of ages was between 42 and 58 The anterior pituitary insufficiency was of the chronic type in all cases A chromophobe adenoma was suspected in one case

The genital dyscrasia was exhibited by,—amenorrhea, impotence, lack of libido and, in two of the male cases, by small size and incomplete descent of the testes. Sexual hair was absent, and the hair of the scalp and eyebrows was absent or scanty. The skin was elastic, soft and moist, no subcutaneous edema was present. The basal metabolic rate was low and could be raised by the administration of thyrotropic hormone.

Five patients had complete achlorhydria, and the sixth hypochloridria Anemia was present in all cases and was considered to be gastrogenous, and due indirectly to the anterior pituitary insufficiency. Three of the six patients showed symptoms of subacute combined degeneration of the cord. In one the hypochronic anemia responded to iron, and the other two cases were of the Addisonian type and responded to liver therapy.

The author's conception of the sequence of the clinical events is,—that besides the usual secondary endocrinous manifestations of anterior pituitary insufficiency, there results an achlorhydria which in turn is eventually succeeded by an iron deficiency anemia, a liver deficiency anemia, subacute combined degeneration of the cord, or a combination of these conditions

SIMMOND'S DISEASE

Simmond's disease or pituitary cachexia was originally reported in 1914, as a case of "Pituitary Atrophy with Fatal Outcome"

The primary endocrine pathology in the condition is atrophy of the anterior pituitary lobe or a lesion such as a tumor, cyst, infectious process, hemorrhage or a pressure process which destroys the anterior pituitary cell function

The condition occurs more commonly in women following pregnancy and especially its septic complications. It is featured by a pronounced, extreme and progressive loss of weight, polyuria, anorexia, headache, amenorrhea in the female and impotence in the male along with the usual loss of normal psycho-Other clinical sexual characteristics features are the loss of hair and teeth: pigmentation, atrophy of the skin, atrophy of the breasts in the female and sexual organs in both sexes; hypoplasia of the thyroid; lowered B M R and blood sugar, tendency to insulin sensitivity, subnormal temperature, atrophy of the adrenal cortex and hypotension, marked mental apathy, irritability, depression and progressive physical asthenia

The impairment or loss of anterior pituitary function results in diminished tropic factor production which causes atrophy of the thyroid, adrenal and sexual glands. Accordingly Simmond's disease and multiple ductless glandular sclerosis. (Falta) have many common pathological and clinical features. Cases with tumors of the pituitary gland and terminate in a collapsic state, the features of which are not unlike the terminal coma (often due to hypoglycemia) observed in Simmond's disease

Therapy—The following preparations have been reported as effecting good results in Simmond's disease despite the generally conceded high mortality rate ordinarily experienced

- 1 Anterior lobe extracts
- 2 The A P. L substances
- 3 Cortin.

Insulm has been recommended and advocated, however, it must be noted that cases of Simmond's disease are insulm sensitive because of their lowered blood sugar level and the increased tolerance for carbohydrates

Personal experience indicates that good results are obtained by the administration of Polyansyn, a combination of the Collin tropic fractions obtained from the anterior pituitary, or the anterior pituitary liquid extract (Armour) in 1 or 2 cc doses given daily, when improvement occurs-weight gain or the skin becomes softer and more pliable, the frequency of administration is then reduced to three times a week. There may and likely will be an early loss of weight before improvement occurs. In conjunction with this oestradial benzoate (Progynon B) is administered intramuscularly in 50,000 i u dosage every five to seven days until pronounced breast enlargement or menses occur, at which time the oestrin therapy is sustained by giving 10,000 i u of estradiol benzoate

If the hypotensive level is extreme and weakness is profound, 1 to 5 cc of cortin is administered and repeated daily or less frequently, according to the needs of the patient. The presence of edema may contraindicate the use of cortin, especially if retention of chlorides is present.

The A P L products have also been administered in 1 to 2 cc. (100 to 200 r tt.) dosage daily or every other day with good therapeutic results

All potent anterior lobe preparations should be suitable for administration in Simmond's disease for in this condition and as previously stated, recoveries have been reported in cases administered these preparations.

General hygienic care, rest in bed and forced elimination are essential to recovery

Prognosis — The prognosis should always be guarded, even in cases manifesting marked improvement, because of the suddenness in which a tatal hypoglycemic attack occurs in this condition

It appears to be most difficult to overcome their insulin sensitivity and to elevate the blood sugar in Simmond's disease after the hypoglycenic attack occurs. The therapy recommended for this state is the intravenous administration of 1 cc of adrenalin chloride solution (1 1000) and in the intravenous administration of 10 cc of 50 per cent glucose solution to be followed by the continuous intravenous administration (40 to 60 drops per minute) of a five per cent glucose solution. If the blood chlorides are normal, the glucose may be administered in saline solution

PINEAL FUNCTION

In an editorial²⁷ in the Lancet it is Experimental evidence of the two functional theories concerning the pineal-Descartes 'seat of the soul and its domain over virility"—is about equal The gland is not essential to life, and experimental extripation of the gland has led to negative results in one series, and to the appearance of macrogenitosomia in others. Tumors of the pineal in young lovs, producing precocious puberty and somatic overgrowth, have been variously attributed to hyper- and hypotunction of the gland Cushing however, attributes the curious syndrome to secondary effects upon the pitintary gland

A J McLean²⁸ observes Pineal tumors, according to Cushing, constitute but 0.7 per cent of all intracramal tumors

Teratomas of the pincal gland are rare, only 25 have been reported in the past century

He reports a case of pineal teratoma in a boy aged six years who complained of headache, vomiting, and failing vision

He was precociously bright, and had always been restless in his sleep. The

gait was normal and he "ran like a deer" His weight had been usually below normal, he had recently lost weight, and was abnormally constipated

He had frequent bouts of severe intertemporal and frontal headache, with sharp prostrating pains during the three weeks preceding his present illness. He had become nervous, had begun to stutter, his voice lost its intonation and after a few minutes' conversation "he would be screaming at the top of his voice." He complained of severe epigastric pains Recently his left eye had turned inward, light hurt his eyes, diplopia and foggy vision were complained of at such times as he could see

Examination showed a small dwarf-like well formed boy, with hyperkinetic reactions. McEwan's sign was positive, and some suboccipital tenderness was present. The teeth were carrous

The genitals were normal. The left and right eye showed 20/66 vision concentric contraction of the visual fields, bilateral choked discs, with five diopters deviation paralysis of right abducens nerve and complete mability to elevate the eye above horizontal

Bilateral absent knee jerks, a positive lett Oppenheim, and a marked sway in Romberg position were present

Cramal roentgenogram showed sutural diaschasis, and moderately advanced convolutional atrophy

Ventriculography showed increased spinal fluid tension and roentgenogram showed a symmetrical internal hydrocephalus and a soft tissue mass projecting downward in the midline from the posterior superior portion of the third ventricle

Operations in successive stages, due to the patient's condition and rapid loss of weight, showed a tumor of the pineal about 28 mm in diameter, which was removed. Death occurred hours later

Necropsy was obtained Microscopic study of the pituitary, thyroid, thymus, adrenal, testes, and pancreas showed normal There was a normal but flattened pineal body. The parapineal teratoma contained tissue derived from all three germ lavers

It is probable that not all tumors reported as pineal teratomas actually arise from the pineal body itself, and this fact is mentioned by Ewing, and it is known that teratomas occur elsewhere in the cranial cavity

Horrax20 records the subsequent history of the cases with pineal tumors reported in the Arch Neurol One) Psychiat 35 215 (Feb.) 1936 adult patient was alive and well 212 vears after operation

The case of pubertas precox had had a recurrence of pressure symptoms which did not respond to the third series of roentgen therapy

By means of a new two-stage operative approach, a histologically verified pinealoma was removed Resection of the right occipital lobe and a portion of the posterior parietal and temporal areas permitted an excellent view of the pineal region

The pinealoma weighed 70 Gm, was nodular, him, and extremely vascular, its measurements were 8 + 45 cm 3 cm. The tumor was composed of typical pineal parenchymal cells

The patient survived operation for three months, death resulting probably from postoperative adhesions that caused a spinal block

> 1/1 Stringer 30 reports a case of parealoma with a metastases of the tumor occurring in the region of the tuber emerum and destroying the tuberal group of hypothalmic nuclei invading the hypopheseal stalk and occluding the infundibular canal

The patient had had diabetes insipidus for a period of five months, which at first responded to pituitary injections, but later it had no effect on the polyuria

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HEMATOLOGY

By WILLIAM DAMESHEK, M D

BLOOD-FORMING ORGANS

The Bone-marrow Biopsy-N Henning¹ reviews the various indications of the sternal bone-marrow biopsy He mentions particularly his success in the diagnosis of multiple myeloma and of malignancy metastasizing to the bonemarrow and refers to the earlier work of Sevfarth and of Schilling in the diagnosis of malaria and kala-azar from the bonemarrow Hans Schulten² also contributes a general review on the subject of bonemarrow hopsy, in which are fully discussed the indications, both investigative and diagnostic, of the biopsy in periicious anemia, thiombocytopenic purpura, and the leukemias. The Reviewer has utilized the procedure chiefly in investigation and it has proved of invaluable assistance in the appreciation of the physiological pathology behind the blood picture. In diagnosis, as pointed out on many occasions, it has proved helpful in unravelling those cases of anemia which have failed to respond to liver and iron and which are usually associated with a normal or high color index and low leukocyte and platelet counts. K. Rohr and R. Hegglin? were successful in finding tumor cells in sternal biopsy material from 10 of 12 cases showing tumor metastases to bones

Technic—G Karavanov⁴ contributes a modified technic for trephining the sternal marrow. Instead of making an meision through the skin and subcutaneous tissues he pierces them by means of a special small trocar, through which the perforating trephine is introduced, after which marrow is removed by means of a small curette. This method seems to have some merit since with it one can obtain not only smears but pieces of tissue for

A Kırschbaum and Hai sectioning Downey⁵ compared some of the methods used in study of hematopoietic tissues and concluded that no better method than sectioning was found for purposes of cellular orientation The simple imprint technic, using dried, stained smears offers definite advantages, however, in respect to both cellular morphology and ease of preparation The Reviewer has had the same experience as well, not only in bone-marrow preparations but in those made from the lymph-nodes and accessible tumors (thyroid. breast, skin, etc) The method of simple imprint and staining with Wright's or Giemsa stain should be more widely used than it is at present

Some of the arguments for and against the trephine vs the puncture technic of bone-marrow biopsy are taken up in a paper by L B Kingery, E E Osgood, and A H Illge 6 These authors recommend simple puncture of the sternum by use of an abbreviated lumbar-puncture needle with subsequent aspiration of a small amount of material with a 10 cc syringe. In a comparative study of the puncture and trepline methods of biopsy, W. Dameshek, H. H. Henstell, and Eleanor H Valentine7 found that the trephine biopsy offered many advantages sections were obtained from which topography could be studied, smears directly from the marrow were received which differed greatly in composition from the fluid removed by aspiration The "puncture" material was considered "juice," mostly blood with a relatively small number of marrow cells It must be conceded that the puncture method is more simple, however, its inaccuracy will probably lead to many errors in diagnosis. Its value in investigative work is debatable since it probably is neither marrow nor blood but a variable mixture of each of these tissues. As a preliminary method of study to the more difficult trephine method, the puncture biopsy probably holds a definite place. If a diagnosis can be obtained in this fashion, all well and good, if the diagnosis is still questionable the trephine procedure might then be used.

Study of Cells-One of the interesting newer investigative methods applied to study of the marrow cells has been that of the fluorescent microscopic technic Porphyrin, the precursor of hemoglobin, develops a red fluorescence in the presence of ultraviolet light and Konigsdorffer (1929) some years ago took advantage of this fact in studying the bone-marrow cells in various abnormal conditions with some particularly interesting results in pernicious anemia, in which they found that many of the megaloblastic cells contained porphyrin They postulated from this that a gross abnormality in the "building-stones" of the red cells existed in the disease K-A Seggel⁸ repeated these observations in both blood and bone-marrow smears utilizing the same technic and found inconstant and very slight fluorescence in the nucleated red cells of permeious anemia, although fluorescence was noted in mature red cells and even in leuko-Hans Muller-Neff' extended these observations on "fluorescytes" and found that fluorescence was present only in young red cells (reticulocytes). This denoted that porphyrm was present during active hemoglobin formation and was therefore important in normal as well as abnormal hemoglobin synthesis. Observations of this type, although admittedly very technical, deserve repetition because of the insight they may give into the physiological pathology of blood forma-

Another very interesting technic applied to bone-marrow cells is that of Walter Kempner¹⁰ who studied (for the first time) the metabolism of human erythroblasts with the Warburg apparatus He was fortunately able to obtain large numbers of nucleated red blood cells from the blood of a case of ervthroblastic (Cooley's) anemia, and showed that the erythroblasts had a very high oxidative and fermentative metabolism, their respiration being approximately 200 times greater than that of normal non-nucleated red blood cells. Indirectly these data indicate the relative lifelessness of the mature non-nucleated red blood cell, which is in reality not a cell but a bag containing a very active chemical—hemoglobin The very high metabolic activity of these immature blood cells is not too surprising in view of the fact that the blood cells are the direct representatives in the adult of the primitive mesenchymal tissue of this type should prove exceedingly interesting in bone-marrow tissue from various abnormal conditions

Methods — The statement has been made that "The day of the colorimeter seems gradually to be passing and in its place is coming the era of the photometer and spectrophotometer that utilize a given wave-length of light for measurements of intensity of an unknown solution" This prediction appears to be becoming an actuality since in many of the more advanced laboratories the colorimeter is being pushed into the limbo of forgotten instruments, as there is increasing realization of its relative inaccuracy. The "stabilized photoelectric colorimeter with light filters" of K. A. Evelvn¹¹ has proved its outstanding accuracy and ease of operation in many excellent laboratories Evelvn's instrument disposes of the errors inherent in the previously used photoelectric colori-

meters and makes possible the rapid reading of concentrations of the various colored solutions used in colorimetry. It does away with the subjective element of the technician's eye substituting for it the photoelectric cell, the fluctuations of which are transmitted to a galvanometer and which depend entirely upon concentration of solution. The accuracy is within ± 2 per cent. To increase this accuracy, various types of color filters may be used for the various colorimetric procedures. Hemoglobin readings are very satisfactorily done with this apparatus

Hemoglobin and Red Cells—() S Walters12 determined to study the variation of erythrocytes and hemoglobin in man during mactivity. They found that rest of one-half hour lowered the hemoglobin about 1 (in and the red cell count about 500 000 Beyond this, there was no fluctuation, either hourly or in response to meals. In this paper, statistical variations were discussed, and these are fully taken up in an important review by P. D. Rosahn 13 Those who are at all interested in the variables which come up in investigative and laboratory work are rightly warned of the value of the statistical approach c I Nelson¹⁴ states quite correctly that the use of single average figures tor expressing normal or standard values is hard to understand. In this paper Nelson again calls attention to the many glaring faults in the percentage method of expressing hemoglobin concentrations in blood. "First of all, there is no agreement as to what value shall be called a standard or 100 per cent value. In the second place, the phrase 100 per cent has no definite meaning" Nelson recommends that since normal individuals vary greatly in their hemoglobin and erythiocyte concentrations, one should speak of normal ranges with their maximum and minimum value Thus, in man, the hemoglobin varies from 12 35 to 18 50 Gm and the red cell count from 4 10 to 6 50 million, whereas in women the hemoglobin range is from 11 00 to 16 80 Gm per 100 cc and the red cell count from 4 00 to 5 50 million

The sedimentation rate continues to receive a large amount of attention In common with various other investigators, K T Sasano, W H Ordway. and E M Medlar¹⁵ determined to study the effect of various factors such as temperature, barometric pressure, manipulation, and anticoagulants on the rate of erythrocyte sedimentation They conclude that minimal and gentle handling of the blood is important as well as the use of an isotonic anticoagulant such as 11 per cent sodium or potassium oxalate Emphasis is placed upon keeping the blood at body temperature since this places the colloidal suspension in an environment approaching the normal Paul Wood¹⁶ contributes an important article on the sedimentation rate in heart disease. He found that congestive heart failure retarded the rate, and that increased rates were present in cases of active rheumatic heart disease, syphilitic aortitis, and invocardial infarction. In the latter condition, the sedimentation rate was found to increase gradually to a maximum at about the end of the third week and to become slowly diminished as the infarct healed. The increased rate is probably due to softening of the myocardium in the region of the thrombosis whereas healing may be inferred when the rate diminishes. The somewhat accelerated rate with angina of rest may be due to multiple tiny areas of myocardial softening The test may be useful from the prognostic and therapeutic standpoints, particularly in settling the vexsome question of when to allow the patient to get out of bed Since coronary disease occurs in the older age groups, it is important to know whether the sedimentation rate becomes disturbed in middle-aged and old persons. I. Miller to studied this problem and found that age had little effect, faster rates were accounted for by various abnormalities as malignant disease, tuberculosis, or cardiovascular disease. H. Reichel to found the sedimentation rate increased in 90 per cent of cases with malignant tumors. Despite the non-specific character of the test, it may thus be of value in distinguishing between the presence or absence of malignant disease.

The mean corpuscular volume as determined by Wintrobe is rapidly coming into greater prominence, as mentioned in previous reviews (W Dameshek¹⁹1 F. L. Dunn and J. C. Sharpe²⁰ state that they have found that the necessary calculations involved were often a source of 'perplexity and error," and propose a series of nomagraphic alignment charts to calculate the various indices. These charts are illustrated in the article and may prove useful to those who do not enjoy the problems of simple arithmetic Hall Schartum-Hansen²¹ points out the very useful fact which we can confirm regarding the direct relationship between the hematocrit (volume per cent of packed red cells) and the hemoglobin content. We have found that one of these observations may be used to check the other-or having one the other may roughly be calculated. Thus, the approximate hematocrit usually may be calculated by dividing the hemoglobin readmg by two

Much dissatisfaction exists with the tragility test which as ordinarily done, has many points of maccuracy E. I. Ponder has devoted many years of work on hemolysius, hemolytic systems, and accurate methods, all of which has been put together recently in a large volume 22

The ordinary fragility test may be made more accurate by careful attention to volume of hypotonic salt solution, volume of the red cell suspension, and the degree of anemia (as measured by the hematocrit). The latter may be adjusted so that one always uses a fairly constant number of cells even when there is marked anemia present which will modify the results. These points are discussed by Geneva A. Daland and Katharine Worthley? I who described a modified method using hypotonic salt solution.

I S Wright and Alfred Lilienfeld²⁴ describe a standardized tourniquet test which is useful in several conditions, particularly in hemorrhagic disease and in source. Instead of recording a tourniquet test as negative or positive as usually done, these authors record the number of petechiae which appear and can be seen by the naked eve in a circle of 25 cm diameter 4 cm below the crease of the elbow. The tourniquet used is the cuff of a blood-pressure machine which is inflated to midway between systole and diastole and maintained at that point for 15 minutes. In this way, the results obtained can be recorded and their variations noted from day to day

related not directly Mthough some mention should be bematology made of gastroscopy which is being used more and more for direct exanimation of the gastric mucosarelationship of disorders of the stomach to anemia has become so well-known that it is no wonder that investigators have become interested in this phase of the problem. Thus C. M. Jones, E. B. Benedict, and A. O. Hampton²⁵ have studied the gastric mucosa in various cases of anemia. An excellent summary article of the subject of gastroscopy is contributed by Jacob Schloss 26 J. G. Cabson, 2nd, and W. A. Evans,

Ir 27 describe a method for the determination of the blood volume in which the azo dye "Evans Blue" is used, readings of the concentration of the dye being made with the spectrophotometer The difficulty of the method and the complicated nature of the apparatus will prevent its general use Although the relative inaccuracy of the commonly used method of Keith, Rountree, and Geraghty is brought out, one wonders whether it is not desirable to continue its use at this time knowing its maccuracies In a companion paper Gibson and Evans25 conclude that no relationship exists in normal persons between variations in total blood volume, venous pressure, and blood velocity rate. The blood volume of normal males is greater than that of females, with increasing age the blood volume declines, muscular and obese individuals have a higher total blood volume, although obese persons have a lower volume of blood per unit of body weight than thin individuals The blood volume of normal individuals varies within wide limits, and is dependent chiefly upon differences in the height and surface area

Certain Chemical Constituents-Normal and abnormal porphyrin metabolism are discussed by Kontad Dobrmer²⁹ and C. J. Watson ³⁰ These investigators are two of the very few in this country working in this difficult but important field. In three cases of lead poisoning, for example, Watson was able to isolate a porphyrm established as coproporphyrin III The anemia and stippling found so commonly in lead porsoning are probably related to disturbances in the porphyrin metabolism J Bence, J Lendvai and J Szekely³¹ studied the copper content of the blood in anemia and concluded that since this element was increased when there was evidence of rapid regeneration of the

red cells, copper probably had a definite action on red cell growth

The metabolism of iron is being studied in several laboratories, although until very recently this was a comparatively neglected field C. E Jenkins and M L Thomson³² after analyzing the various methods for the determination of blood iron, describe their own, both for whole blood and for plasma This is a colorimetric test but apparently exceedingly accurate in the authors' hands It is in agreement with the spectrophotometric investigations of other workers Jenkins and Thomson found that women had more plasma iron than men, and that this was probably due to increased regenerative activity induced by successive menstruations Furthermore, in preliminary studies of the anemias, the plasma iron was found to vary considerably and is therefore of some significance The total blood iron was found to be greater than that which could be accounted for by any known method of estimating the hemoglobin concentration, the average non-hemoglobin iron normally was about seven per cent C V Moore, W R Arrowsmith, J J Quilligan, Jr, and J T Read B write along the same lines. Iron, they state, is recognized in three forms in the blood hemoglobin iron, plasma iron, "easily split-off" iron (The latter form is readily freed from its lightly bound state in the red cells and plasma by weak acids.) The various criticisms of the plasma-iron methods are discussed and the techniques necessary to avoid their maccuracies described Normally 50 to 180 micrograms (thousandths of milligrams) of non-hemoglobin iron are present in 100 cc of human serum Barhan's "easily split-off" iron is discussed together with a method for its determination This gives figures indicating that approximately five to ten per cent of the whole blood iron is "easily split-off" from its usual combination by the action of dilute acids. Whether or not it is non-hemoglobinous iron is debatable In a companion paper, C V Moore, C. A. Doan, and W. R. Arrowsmith34 present some exceedingly interesting and extensive observations on the relationship of these forms of iron in various cases and types of anemia In the iron deficiency states the plasma iron was very low, in pernicious anemia very high Otherwise, it was very labile, being readily influenced by many factors and thus corresponding to simple "transport" iron Iron in other words is transported from tissue to tissue as plasma iron, this is influenced by gastrointestinal absorption, the iron reserves in the body, the ability of the bone-marrow to utilize iron, the rate of hemoglobin synthesis, the degree of hemolysis in the spleen and other tissues, and other factors. The physiological function of the easily split-off iron was not deternined

Genevice Stearns and J. B. Mc-Kinley 12 performed iron balance studies in early intancy and found that a daily loss of 1.25 mgm of iron from the body occurred in artificially fed infants up to two months of age (about 50 to 75 mgm m all). Thus a dietary source of non is desuable, the authors conclude, well before six months of age inless human milk is given. In a companion paper, these authors G Stearns I B McKinley, and D. Stinger 10 conclude that neither egg volk nor spinach increased the non-retention which was. however definitely increased when the infants were given a special iron-rich cereal or ferrie ammonium citrate

Ruth M Leverton and Lydia J Roberts³⁷ made a careful study of the iron metabolism of normal young women during several consecutive menstrual

cycles It was found in these studies that the subjects lost an average of 14 26, 22 84, 11 13, and 13 80 mgm, of iron corresponding to 30, 51, 26, and 30 cc of blood respectively during each menstrual period. The average daily intakes of iron were 13 61, 11 87, 10 03, and 11.71 mgm. These studies suggest that the low hemoglobin values which are accepted as normal for women may be a direct reflection of the use of diets too low in iron for the drain of menstruation.

P F Hahn³ reviews the entire subject of iron metabolism and points out the many difficulties in the field C W Heath and A J Patek, Jr ³⁹ discuss the subject in relationship to the anemia of iron deficiency (q. v.)

Blood Cells

General-K Kato40 has performed a worthy service for both the clinician and technician in putting together in simple tabular and pictorial form the origin, development and interrelationships of the formed elements of the blood The resultant schema is easy to follow and has been a particular boon to techmeians. Despite the simplicity of the colored lithograph and tables, accuracy is not sacrificed. The monophyletic schema of blood cell formation is utilized. all cells being derived from the primitive mesenchymal cell, this in turn produced "mycloblasts" which in turn give rise to various types of erythroblastic and leukoeytic cells. In a paper by () C Hansen-Pruss⁴¹ the blood cells are studied by the infrequently used technique of dark-field illumination author claims that "the method avoids the involved and somewhat unreliable technical factors encountered in the use of the supravital dyes and in staining of fixed smears" Apparently malarial parasites are well brought out with this

method, which may prove to have a very limited value P D Rosahn and A E Casey42 in a very careful study compared the quantitative variations in the "hemacytologic constitution" of healthy men and rabbits. The blood formula of both these mammalian types differed widely from individual to individual, indicating that there might be an inherent or constitutional variability blood-cell formula normal for one individual may in fact be abnormal for another This is of particular importance, the reviewer has found, in estimating whether leukopenia or leukocytosis is present in a given case. Individuals vary so widely in what is their normal, that one should not immediately jump to a conclusion that a count of 5000 white blood cells per cu mm is leukopema or that of 12,000, leukocytosis. This holds true as well for the differential percentages of white cells

Red Blood Cells-Ruth VI Leverton and Lydia J. Roberts43 studied the daily variations in hemoglobin and red cell counts with particular reference to the menstrual cycle in four normal college women. This work which was done as part of a complete study on the non metabolism brought out clearly the occurrence of daily variations in both hemoglobin and red cells which were apparently unaffected by the menstrual process. The writers point to the difficulty involved in making generalizations from single observations, when rather marked daily variations are normally present. The REVIEWER can confirm this statement especially when such abnormal states as permicious anemia are followed from week to week, variations here are even more difficult to interpret The factors of technical error, I find, are insufficiently recognized by the profession at large, which often accepts at

face-value the printed reports from a technician or technical laboratory.

Hans Langendorff and Alfred Reisner44 studied the normal reticulocyte count in man and concluded that the figures usually given of 05 to 1 per cent are much too low, their average figure being 11 to 17 per cent (!) The daily variations which are present are dependent upon the "normal rhythm of the biologic milieu" Although these conclusions are interesting, it seems strange that so many workers in widely separated laboratories have reported normal values which are under one per cent. As for the existence of daily variations. these are doubtless correct, but their clinical value is questionable E Jacobsthal⁴⁵ makes the interesting observations that in a new malarial infection it is the reticulocytes which are chiefly infected, not the mature red cells. Ninetv to 98 per cent of the infected cells are reticulocytes this being the case, anemia more readily develops since the younger cells are being destroyed

Blood Transfusion-Much is being written nowadays about blood transfusions. The Russians have their institutes of transfusion in which are kept on hand large quantities of blood of the various types ready for immediate use As is well known, the Russians have pioneered the use of cadaver blood, which as yet has failed to find favor in this country The chief contribution of the Russian school is, however, that of storage of the blood for a period up to two weeks, possibly longer Beyond that period, the plasma is utilized for other purposes The French now have their central clearing stations where blood of the various types is kept on hand for the different hospitals ready for instant use. In Chicago, at the Cook County Hospital, a "blood bank" has been set up, which performs the functions of collecting all available blood and of dispensing it on call (What a relief this must be to long-suffering internes and technicians used to many hours of work in typing and cross-matching many hundreds of donors!) In all fairly large hospitals, some effort might well be made to conserve blood which is frequently wasted and have it readily available for transfusion purposes. The blood from patients with hypertension, right-sided heart failure, and polycythemia might well be utilized Large quantities of polycythemic blood are routinely used at the Beth Israel Hospital (Boston) for transfusion G W Pickering40 has found that blood from patients with hypertension is similar to normal blood in its content of pressor and depressor substances and is thus useful for transfusion. It is well to point out, in many discussions of transfusion, that this procedure is often too lightly entered into and without definite indication A V Bock⁴⁷ summarizes the sate and sane attitude in transfusion and lists indications RIVIEWIK finds that too often transfusion is done as a gesture or as a 'filler' to take up time during anxious hours when 'something must be done' Frequently, more harm than good is done, particularly when reactions develop. Reactions are all too common, these may be due not only to incorrect typing but to other disturbances resulting in chills and tever compatibility tests are not enough, in addition, both patient and Jonor should be typed. Except in very rare instances this will avoid the tragic experiences which occur all too frequently Occasionally intra-group reactions will occur as described by C. G. Culbertson and A. W. Ratcliffe 48. In this case, both the recipient and donor were of Group () (Type IV, Moss), but a very severe renal reaction occurred, almost resulting tatally. Hanging drop

compatibility tests were repeatedly negative but by the test-tube method or the centrifuge test method49 it was found that the patient's serum agglutinated the donor's cells and also 22 or 23 other Group () (Type IV) donors Except in two instances the hanging drop method failed to show agglutination. Because of this and another experience, Culbertson and Ratcliffe now utilize the following routine procedures in choosing a blood donor (1) grouping the patient with test sera, (2) cross-matching-recought's serum with donor's cells and donor's serum with recipient's cells by both hanging drop and centrifuge test methods, (3) Kline test of the donor They state that although this routine may sound cumbersome, it has not slowed up the laboratory service. Except in extreme emergencies, one can never be too careful even at the expense of a little more time lost. The ordinary transfusion reactions are not, however, dependent upon blood group phenomena but are due to non-specific protein reactions, which are probably due in great part to technical errors A N Filatov, N Blmoy, and M. Depp⁵⁰ recommend the following precautions for reducing the incidence of these reactions (1) careful cleansing of the apparatus for blood transitision (2) prevention of blood clotting (3) observance of painstaking asepsis, (4) maintenance of proper temperature of the blood, (5) using distilled water free from any impurity for the solutions of chemicals

Many new modifications in the transtusion of blood are being made. The use of preserved blood has been referred to above and is being rapidly taken up all over the world. All the authors testify to its quick availability in emergencies and to its safety, particularly if the blood has been preserved at a constant very low temperature (33.8 to 39.2.1° or

1° to 4° C) and if it is used preferably within a week. In the treatment of severe hemorrhage as from peptic ulcer, Marriott and Kekwick, and I J Wood⁵¹ have successfully utilized the method of continuous intravenous blood transfusion This has proven of far greater value than the continuous infusion of large quantities of saline and dextrose solutions and has often led to dramatic improvement in physical status and hemoglobin percentage Citrated blood was given at the rate of 99 to 150 cc an hour and for 12 to 48 hours A Fonio⁵² suggests the use of fractional blood transfusion-red cells or platelets as needed in the individual case The erythrocytes can be used for anemia, the platelets in thrombocytopenia, and the plasma in fibrinopenia or for increasing the blood proteins Fonio has had no personal experience with this method, which, however, appears to be of some practical value. The REVIEWER has given platelet transfusion in thrombocytopenia, but great care must be taken in the handling of platelets to prevent the formation of thrombi P Hedenius 33 suggests the novel method of heparinizing the donor, and thus being able to transfuse the patient at leisure and without worrying about coagulation. For once the donor is considered in an article Israel, and A Merklen, L lix Applel 34 who studied the effect of frequent venesections in professional donors. The hemoglobin concentration was reduced in several and there was a tendency to leukopenia and neutropenia Regeneration after venesection is fastest in the crythrocytes, slightly less rapid in the hemoglobin, and still slower in the white cells

White Blood Cells—Many articles are still being written extolling one type of diagnostic or prognostic test above all others in an acute infection. The

conservative view to take, it would seem. is that a test like the leukocyte count. differential count, sedimentation rate. etc., is of value only as an added symptom In tuberculosis, for example, J K Miller⁵⁵ wisely writes that the ideas regarding prognosis, degree of activity, and efficacy of therapy cannot be obtained simply by taking one test as a criterion, but by consideration of a series of successive correlated studies of the Schilling test, blood sedimentation rate, and monocyte-lymphocyte ratio These procedures may be of aid in demonstrating the presence or absence of pathologic activity. H J Rinkel⁵⁶ describes his experience with the "leukopenic index" which was devised by Vaughan for the study of "food allergy" Theoretically, if a subject is hypersensitive to a given food, the bonemarrow will react with the production of a leukopenia, leukocytosis otherwise results Rinkel confirms Vaughan's observations regarding the misleading character of clinical impressions and skin tests in food allergy

Michael Zeller⁵⁷ studied very carefully the reaction of the leukocyte count to rest, mild activity, violent activity, and after light and heavy meals. Under basal conditions and with complete rest, the white cell count in his subjects did not vary more than 750 cells per cmm Iven mild activity caused increase in counts up to 2400 cells per cmm A heavy meal caused marked increases in counts (from 2400 to 5100 cells per cmm in five subjects) Zeller concludes that if the conditions for studying the leukopenic index are rigidly maintained the test should be of definite value T L Squier and F W Madison⁵⁸ state that an eosinophilia may be correlated with the appearance of leukopenia following allergenic foods in hypersensitive individuals. The eosinophiles were counted directly in the hemacytometer by the use of an acetone-eosine diluting fluid. Although eosino-philia was said to occur very commonly, the increase in eosinophiles in 86 instances among 200 tests was 200 cells per cmm. or less Since this degree of increase represents the presence of only one cell per total sq mm in the hemacytometer, and since no precise description of how squares were counted, etc, is given, the results are to be accepted with much skepticism until they are adequately confirmed.

Platelets - Too often the platelet count is neglected in hematological studies This is mainly due of course to the relative difficulty of technic and to lack of any standardized method. In our own laboratory, satisfactory results have been obtained since 1930 with the use of an "indirect" method in which the fresh blood comes in contact with sodium citrate and brilliant cresvl blue 59 I Olef60 uses a somewhat more difficult but also "indirect" method The normal platelet counts with both of these methods range between 400,000 to 800,000 per cmm A reliable index of bone-marrow activity may be obtained from study of (1) the total leukocyte count, (2) the polymorphonuclear percentage, (3) the reticulocyte count, and (4) the platelet count Reduction in blood platelets is often the first sign of serious disease of the bonemarrow and may antedate all the other signs above enumerated. Oleto1 has also studied the differential platelet count and has divided the platelets into four groups depending upon their size. The smaller platelets are much more active tunctionally than the larger types ("Giant platelets are dwarves in function") Increased numbers of large platelets are seen in various functional abnormalities J Arneth, whose exof the marrow haustive encyclopedic treatises on the various qualitative changes in the leukocytes during infectious disease were so complicated that they were neglected for many years, now appears to be doing the same for the "qualitative thrombocyte picture" in a series of ponderous and extremely detailed articles, each article being devoted to one disease. 62, 63, 64 Arneth continually stresses that the qualitative platelet reaction like that of the erythrocytes or leukocytes, is a true biological reaction which should give a particularly good insight into various pathological conditions H. Zondek and R Kaatz⁶⁵ conclude that the blood platelet count is considerably influenced by the thyroid and thyrotropic hormones They were able to increase the platelet count in normal individuals by administration of those substances I Olefo6 showed that large platelets are more mature than small ones and disintegrate more rapidly than the younger forms In infectious and postoperative states the platelets are increased in number and exhibit an increased fragility which might be of significance in the pathogenesis of spontaneous venous thrombosis

W H Howell and D D Donahue⁶⁷ describe first a new method for the determination of the platelet count heparimized buffer solution was used for the diluting fluid, the counting being done in a hemacytometer. Since it was found that arterial blood gave higher platelet counts than venous blood, it was thought that this might be due to an increase in platelets during the passage of blood through the lungs. This point was made the subject of a special study by experimental and histological methods, which showed giant cells ('megakaryocytes") in the lungs. Although giant cells have been found in the lungs before, they have been interpreted as being screened out of the blood and arising from the marrow Howell and Donahue

TABLE I

RELATION OF BLOOD FINDINGS TO RED CELL FORMATION AND DESTRUCTION

| Active bone marrow | Increased number of reticuloytes, basophilia, nucleation Slight increase in mean erythrocyte volume if reticulocytosis is marked. Often an increase in leukocytes and platelets unless destruction is more active than normal. The number of cells is increased. |
|--|--|
| Inactive hone marrow | Decrease or absence of reticulocytes, basophilia and nucleation. If blood destruction is normal or increased, the cell count decreases |
| Increased red cell and hemo- globin destruction | Increase in bilirubin content of plasma, decrease in number of cells unless compensated for by increased marrow activity |
| Decreased hemoglobin destruc- tion | { Decrease in bilirubin content of plasma |
| Deficiency in crythrocyte maturing factor (permicious anemia) | Anemia with increase in mean erythrocyte volume (increased volume index) |
| Deficiency in iron (iron defici- ency anemia chrome hemor- rhagic anemia) | Anemia with hypochromia of red cells (decreased color index) microcytosis (decreased volume index) if hypochromia continues |
| Hemolytic anemia | \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ |
| Anomia due to decrease in amount or activity of mar- tow (aplastic or hypoplastic anomia) | Anoma with cells of normal size and hemoglobin content, decrease in reticulocytes |
| | 1 1 1027 |

(Courtesy Tournal Laboratory and Clinical Medicine Leb. 1937.)

teel, however, that they originate in the lungs and are active in the production of blood platelets there. The megakaryoexte constitutes, so to speak, a unicel-Inlar gland which gives off a solid secretion in the form of platelets" Although these views of Howell and Donahue are novel and quite radical and therefore in need of confirmation, the observations are so painstaking that they must be respectfully considered E. M. Medlar68 believes that megakaryocytes are found much more commonly in the peripheral blood than is supposed and indicates a series of transition forms in their maturation. The article is well illustrated with excellent photomicrographs, although the REVIEWER is not convinced about the correctness of Medlar's contentions regarding some of the small cells which are called immature mega-karyocytes. These may be atypical monocytes. Furthermore, the well-known tendency of platelets to collect around monocytes may be responsible for some of the pictures suggesting platelet formation from so-called megakaryocytes.

Anemia—The Reviewere has indicated that the old conceptions of "primary" and "secondary" anemia are unnecessary in view of the fact that all anemia is secondary to some cause whether or not this is readily discernible. The conception that anemia is in many instances due to a deficiency in either iron, "liver extract," vitamin B,

etc. is rapidly growing. The old classifications have to great extent been superseded by one based on cell size macroextic. microcytic, normocytic, which the REVIEWER feels should be complemented by etiological factors. Thus: microcytic (hypochronuc) anemia hemorrhagia, achlorhydria, dietary inadequacy every case presenting anemia, it is important to inquire into the question of possible dietary, gastric, intestinal, and hepatic factors, as well as in those of chronic hemorrhage, pregnancies, etc R L Haden⁷⁰ contributes a fascinating article on the mechanism of anemia which is illustrated with many exceedingly graphic charts illustrative of various The charts stress the anemic states rates of red cell formation and delivery from the marrow, the rate of destruction, and the balance between these two factors From knowledge of various hematological and chemical factors such as icterus index and urmary urobilmogen, one can gauge pretty accurately the status of the marrow. Haden contributes the table on preceding page on the relation of hematological findings to red cell tornation and destruction

Chronic Iron Deficiency States (Chronic Hypochromic

A marked deficiency in non-will result in gray han wrinkled flabby skin sores at the corners of the mouth a reddened attrophied tongue and abnormally flattened finger nails as well as in a diminution in the hemoglobin of the blood relative to the red cells, which therefore become small and hypochronic. The REVIEWER in the above paper (thid) has stressed the importance of various dictary, gastrointestinal, and hemotrhagic factors. Achierhydria is commonly present in most of the cases of chronic ("idiopathic," "primary") anemia. C

W Heath and A J Patek, Jr. 71 contribute a comprehensive review on the anemia of iron deficiency, in which the subjects of iron metabolism, "idiopathic" hypochromic anemia, anemia of blood loss, chlorosis, etc., are thoroughly dis-Adelaide P Barer and W B Fowler⁷² found by means of iron metabolism experiments that patients with achlorhydria retained less iron from a normal dietary intake of iron than patients with free HCl in the gastric contents. This might be a factor in the etiology of certain cases of chronic hypochromic anemia F Kellogg, S R Mettier and Katherine Purviance⁷³ attempted to determine the relationship between diet and digestion in hemoglobin production of experimental animals. When anemia was induced in dogs by bleeding, the feeding of beef resulted in a marked rise in hemoglobin output. When the stomach was removed, however, hemoglobin regeneration was greatly reduced these experiments it would appear that once an anemia is induced and the iron reserves depleted, this state will continue if the normal gastric secretion is lacking Erik Mogensen⁷⁴ discusses the anemia of gastric caremonia and concludes that the main causes are undernutrition and failure of the antianemic activity of the stomach

Chlorosis which is a chronic iron deficiency state seen in young girls and of ill-defined ctiology has not disappeared, although its incidence has diminished. This diminished meidence may, however, be more apparent than real, since blood counts between 1870 and 1900 when the disease was at its height were relatively few and diagnostic hematological methods even more recently were often madequate. Often any young girl who was pale was called chlorotic I Olef contributes an article on chlorosis in which observations on three cases

are cited. The gastric juice may show hypochlorhydria or complete achlorhydria, the blood protein may be much diminished, the red cell is smaller and thinner than normal, and the platelet count may be greatly elevated A table is presented in this paper differentiating chlorosis and primary hypochromic anemia Although many minor points of difference may be pointed out, continued observation of cases of both "diseases" has convinced the REVIEWER that they are both examples of a chronic iron deficiency state occurring in different age groups and presenting essentially similar physical and hematological findings. The slight differences in physical status of the patients may be due to differences in age. It has been interesting to watch the development of the physical signs characteristic of chronic hypochromic anemia in cases previously diagnosed as chlorosis at an earlier age group

Treatment—J F Brock 76 and J F Brock and Donald Hunter⁷⁷ contribute important articles on the relationship between the hypochronic anemias Evidence is presented in these papers showme the greater effectiveness of an excessive dosage of non-although no definite explanation for this can be given. Some cases require tremendous dosage of iron, although many require only small dosage Brock found that terrous sulfate in dosage of about 15 grams daily was usually optimal, in addition a diet rich in "firstclass" protein and vitamins should al-The REVIEWER ways be insisted on agrees with these statements except that it is not necessary except prophylactically to give a high iron, high vitamin diet Brock and Hunter found that when large doses of iron are given, large quantities of iron are retained, the retention being much greater than can be inferred from the rate of hemoglobin response. It is likely, of course, that various tissues other than the bone-marrow are more avid for the storage and use of iron than the bonemarrow itself. F. W. Schlutz, Minerva Morse and Helen Oldham⁷⁸ found that in the hypochromic anemia of infants additional iron, when supplied by puréed spinach or apricots was not utilized but that iron salts (ferrous sulfate or ferric ammonium citrate) caused marked increase in the retention and a rise in hemoglobin C A Elvehjem, Dorothy Duckles and Dorothy R Mendenhall⁷⁹ continue to emphasize Elveh-1em's contentions regarding the value of copper in the treatment of anemia particularly of children They present clinical cases of hypochromic anemia in infancy which are said to show that "iron alone is incapable of raising the hemoglobin content to the average level and that supplemental copper is necessary to stimulate an aptimum response" Analvsis of several of the charts in this paper must cast some doubt on the validity of the authors' contentions. It is the RE-VIEWER'S feeling that copper is best reserved for adult practice and then only for the very occasional case which does not respond maximally to large doses of iron. Why subject infants to a chemical which may later do harm to important organs as the liver? Most observers are now in agreement that the ferrous preparations, prevented from being oxidized to the ferric form, are preferable because they require smaller dosage than the ferric preparations and tend to give fewer reactions. Ferrous sulfate is the product now in greatest use, although since the medical pendulum, particularly in hematology, swings so rapidly, styles may be changed without notice Reznikoff and W F Goebel⁵⁰ studied ferrous gluconate in the treatment of hypochromic anemia in rats, apparently as a preliminary measure to its employment in the hypochronic anemia of man The virtue of this preparation lies in the fact that it may be given intramuscularly without undue reaction. However, several studies have shown that only very small amounts of iron salts may be given parenterally, far smaller usually than the optimal oral dose.

Chronic Liver-Extract Deficiency (Pernicious Anemia)

Liver extract deficiency results in gray hair, smooth tongue, gastrointestinal disturbances, central nervous system phenomena as well as in the bone-marrow changes which lead to the hematological picture of macrocytic, hyperchromic anemia with leukopenia and thrombocytopenia which are characteristic of pernicious anemia. In a paper on the status of the bone-marrow biopsy in the disease, William Dameshek and Eleanor H Valentine⁸¹ conclude that two types of erythrogenesis may be present one a normoblastic, the other a megaloblastic, the latter being associated with the "liver extract deficiency" state and observed in only that condition. So-called megaloblasts observed in other conditions are probably immature normoblasts other point stressed by these authors is that not only is the red cell tissue affected in the disease but the white cells and megakarvocytes show marked changes which undoubtedly account for the leukopenia and thrombocytopenia of the blood In other words, there is a "panmyel-With liver extract opathy" present therapy, the complexion of the bonemarrow is rapidly changed to a normoblastic status and within a week after therapy has been started one is hard put to differentiate the marrow from that of normoblastic hyperplasia scen in an active normal marrow following hemorrhage, etc

T. G. Klumpp82 contributes an historical paper on the development of thought on the etiology of pernicious anemia. Juda Groen and Isidore Snapper83 discuss the importance of dietary deficiency as a cause of macrocytic anemia and point out that a clinical picture closely resembling pernicious anemia may at times be caused by prolonged and pronounced dietary deficiency. The gastric juice may contain free hydrochloric acid in these cases and the patients may respond to an adequate diet containing sufficient protein and vitamin B without liver Castle and co-workers pointed this out some years ago in their work on sprue and the Reviewer has emphasized this point, most recently in the article above referred to 84

Svend Petri, D. Bøggild, A. Søeborg-Ohlsen and O Wanscher 5 continue their important experimental work on gastrogenic anemias induced by extirpation of the stomach in swine A hypochronic microcytic anemia was induced. but a macrocytic hyperchromic anemia did not develop after a year of observation as in the work of Bence S M Goldhamer⁸⁶ found that the amount of "intrinsic" factor of Castle was present in greater quantity in the induced remission of pernicious anemia than before therapy Previous observations of this investigator have demonstrated that there is not a total lack of intrinsic factor but rather a marked diminution in association with the marked diminution in The exact the total volume of juice nature of the intrinsic factor or enzyme has not yet been elucidated, although work is now in progress on this point Thus () M. Helmer and P. J. Fouts⁵⁷ were able to separate the intrinsic factor in a relatively pure state from the other gastric enzymes. One awaits the conclusion of their work with interest Fritz Lasch88 was dissatisfied with the cumber-

some method of testing a gastric juice for "intrinsic substance" by incubating the juice with protein, then feeding it to a case of pernicious anemia in relapse with observation of the reticulocyte response. He therefore set out to discover a more rapid method by direct chemical testing of the gastric secretion Normal individuals showed a thermolabile, protem-splitting enzyme which was independent of trypsin or pepsin, this was absent in most of the cases of pernicious anemia studied, although in remission, small amounts of the enzyme might be found. This looks like an interesting test which may prove useful in the differential diagnosis of certain cases of macrocytic anemia

H Vlados, A Bagdasarov, M Dulem and E. Bondarenko⁵⁰ in experimental gastric resection in dogs found that the anemia which developed varied in type depending upon some "constitutional" factor as yet undetermined. Resections of different portions of the stomach indicated that Castle's factor was produced both in the fundus and pylorus and was probably a terment, not a hormone J Bence⁹⁰ found that following total gastrectomy in dogs a microcytic hypochromic anemia at first developed gradually becoming modified in one or two years to a megalocytic, hyperchronic anemia with all the other features in the blood and bone-marrow of permeious anemia Garnett Chenev⁹¹ concludes on the basis of treating patients with permeious anemia with a mixture of liver extract and duodenal mucosa, that Castle's "gastric" factor is present in the duodenum in a concentration equal to or greater than that in the stomach This is in line with the work of E Meulengracht92 who showed that the "pyloric gland organ" (presumably producing intrinsic factor) might be present as far down as the middle of the small bowel The presence of active tissue in the duodenum would explain the failure of case of human total gastrectomy to develop pernicious anemia. Cheney prefers to consider pernicious anemia as due to a combined gastroduodenal defect. It is probably better, however, as noted above, to consider that the disease is the end-result of several different types of abnormalities which in many cases are combined.

Pathology and Symptoms — O P Jones⁹³ in a preliminary paper, reports studies of biopsied pernicious anemia bone-marrow during relapse and makes the point that the entire marrow is involved ("panmyelopathy") Not only is the red cell series affected with proliferation of megaloblastic cells, but abnormal leukocytic and megakaryocytic growth takes place Similar studies, together with a correlation of the blood and bone-marrow picture both in relapse and following induced remission by liver extract are described by William Dameshek and Eleanor H Valentine 94 In this paper, a sharp line of demarcation is drawn between the "liver-deficient" type of crythroporesis (megaloblastic) and the normal and non-deficient type (nor-The "total" character of moblastic) the bone-marrow involvement is also emphasized D Hoffmann⁹⁵ in studying the white blood cell picture in the discase concludes that liver extract acts not only on the red cells but on the leukocytes as well. If the platelets had been studied, the same conclusion would have been drawn regarding this blood element In other words, "liver-extract deficiency" brings about changes in the red cells, white cells, platelets, hair. tongue, gastrointestinal mucosa, central nervous system Great variations in the localization of the deficiency are present from case to case This is well brought out in the central nervous manifestations J F Tourreilles and P C Vazquez⁹⁶ discuss this great variability and describe a case with marked involvement of the posterior columns of the spinal cord in the cervical region. H Cohen⁹⁷ describes two cases of optic atrophy which preceded by a considerable period the clinical manifestations of pernicious anemia and which were quickly benefited by treatment with liver extract. The Reviewer has also observed two such cases.

Treatment - Several groups of investigators continue their attempts to demonstrate the exact nature of the antipernicious anemia principle Υ barow, B M Jacobson and C Fiske95, 99 have already isolated a number of different fractions, and it is probable that some of these fractions exert a primary or initiating therapeutic action whereas others augment and complete the reaction In their last paper, fractions H and I are described together with their clinical activity in cases of permicious anemia (It is to be noted that in this paper no mention is made of assaying the extracts by the use of guinea pigs) A somewhat similar fraction has been isolated by the Scandinavian investigators, Per Laland and Aage Klem¹⁰⁰ and has been clinically tested by B Strandell, L. Paulsson and H. Schartum-Hansen 101 A "good antianemic effect" was obtained by use of an aqueous solution containing 0.7 mgm (1) of this fraction H R Jacobs¹⁰² claims that liver extract which is 'red" contains the 'red substance" of Raper, this is a definite substance which can be isolated from a mixture of tyrosin and tyrosinase Feeding of a preliminary extract of this substance prepared from potato scrapings mixed with tyrosin to a patient with pernicious anemia is said to have induced a very slight reticulocyte response (28 per cent to 60 per cent, the red cell

count being 10 million) Jacobson's work on assaving liver extract on guinea pigs has already been referred to and was commented upon in last year's review Goodman, Geiger and Klumpp found the guinea pig reticulocyte to be altogether too unstable and reactive to nonspecific substances to warrant conclusions with regard to liver extract assays W H Bachrach and S J Fogelson^{10,3} also failed to confirm Jacobson's work and stated that "in our hands the guinea pig was not a suitable animal for assaying antipernicious aneinia potency of liver extracts" As yet, no "laboratory animal can supplant the human permicious anemia patient for the assay of liver potency in the treatment of pernicious anemia"

The number of extracts of liver for clinical use is becoming bewildering One often wonders why the pharmaceutical houses go to such pains to produce, concentrate, refine and advertise their extracts in view of the relative scarcity of cases of permicious anemia. This is probably due to the fact that injections of liver extract are given almost indiscriminately for any case presenting anemia, whether this is hemorrhagic, nephritic, or leukemic in origin reality liver extract is of value only in liver-extract deficiency states (permeious anemia and related conditions). Its use following hemorrhage, in the chronic iron deficiency state and in other conditions is wasteful of the patient's finances and of no value whatever to the patient In permetous anemia, the type of extract to use and its dosage must depend upon the individual patient and the individual preferences of the physician Almost any mjectable extract on the market will produce a satisfactory reticulocyte and envilrocyte response provided it is given in sufficient quantity It is true that some extracts far exceed in potency some others, but with present

day concentration large amounts of active principle can be given in relatively small total amount of solution In neurological pernicious anemia larger and more frequent doses of parenteral extract must be given for successful results H H Hyland and R F. Farquharson¹⁰⁴ recommend in addition that the patient be kept in bed during the early months of treatment Reactions to liver extract sometimes occur, and these may be coped with by desensitization procedures or by changing to an extract from a different animal Most extracts are made from pig liver Campolon (Winthrop) is derived from beef liver and Chappell Liver extract from horse liver

C C Sturgis and Raphael Isaacs¹⁰⁵ describe their experience in treating 600 patients with pernicious anemia in a period of 8+ years The two fundamental principles underlying the treatment of pernicious anemia are (1) administer a highly potent therapeutic agent, (2) give a sufficient quantity to maintain the red cell count constantly between 4.5 and Sturgis and Isaacs state 5.0 million that oral Ventriculin is the method of choice in the majority of patients, but it must be said that this is in contrast with the methods of the Lastern clinics which in most cases use liver extract parenterally, and very seldom, if ever, use Ventriculin. With intection, the dosage of extract should be increased 50 to 100 per cent. Dilute HCL is rarely necessary and its value is questionable fusions of blood may be given if the red cell count is below 10 million. The dietary habits of the patient should be investigated and, if queer, should be rectified Iron may be given if the color index becomes less than one with liver therapy, its value is, however, questionable Sturgis and Isaacs do not recommend bed rest for cases with neurological pernicious anemia since the symptoms

may become aggravated The Reviewer is also of the same opinion P. J. Fouts¹⁰⁶ in an article on the treatment of pernicious anemia states that most patients with the disease require weekly injections of liver extract for maintenance This has been the REVIEWER'S experience as well The patients readily controlled are usually well maintained on oral extracts and are seen only occasionally Those difficult to control. and particularly those with neurological symptoms, must be treated once weekly as a rule, although in some cases an injection every two weeks An analysis of may be sufficient the causes of death in treated pernicious anemia is made Forty-nine per cent died of complications associated with lesions in the central nervous system (bladder, urmary infections, etc.) The remaining cases died of various causes common to the age group A H Sellers¹⁰⁷ made a study of the objective efficacy of liver therapy in pernicious anemia based on recorded mortality data It is generally agreed that although before the advent of liver therapy the average duration of life after diagnosis was about 21/4 years, now with adequate use of liver a fatal termination may be indefinitely postponed in the majority of cases. Analysis of actual mortality figures by Sellers shows that an abrupt alteration in the trend of mortality from pernicious anemia occurred in 1927 coincident with the general introduction of liver therapy The net increase in the average age at death in Ontario in 1934 amounted to 52 years

Other Types of Anemia

The anemia in *pregnancy* was studied by J A Boycott ¹⁰⁸ Cases were equally divided in those with normal and those with subnormal color indices. The cases with normal color index might be due to

simple dilution of red cells dependent upon an increased plasma volume which is irreguarly present in pregnancy. Those cases with a low color index belong to the iron deficiency group and respond readily to iron F. H Bethell¹⁰⁹ contributes an important article on the hematological changes in pregnancy in which he criticizes the views of M B Strauss¹¹⁰ that the anemia of pregnancy can be simply classified in two types an iron deficient (hypochronic) and a "liver deficient" (pernicious) Bethell contends that there are cases which do not respond to iron and which are not macrocytic but normocytic These cases are usually associated with a low serum albumin level and respond to a high protein diet The Reviewer can confirm these data of Bethell's in a few cases On the other hand, it is important to recognize the macrocytic (pernicious) type of anemia in pregnancy in its incipiency, because these cases may go rapidly downhill and are exceedingly refractory to even very large doses of parenteral liver extract

Katherine O'Shea Elsom¹¹¹ reports some careful studies in which the dietary content of vitamin B in pregnant women is correlated with the degree of anemia Patients with deficient vitamin B in their diet invariably developed anemia which was characterized by an increase in the mean cell volume and macrocytosis. The gastric acidity, contrary to the reports of Strauss, remained unchanged Certain clinical phenomena such as glossitis, impairment of vibration sensation, tachycardia, edema and gastrointestinal systems were commonly present Brewer's veast or liver extract produced relief from all the characteristic changes In the pregnant women with adequate vitamin B in the diet no anemia developed An occasional case is seen of normocytic anemia (not macrocytic) which does not respond to liver extract, iron or vitamin

B These cases may occasionally require transfusion, although it is possible in most instances to carry the patient along on liver, iron and vitamin B until about the eighth month when the anemia usually spontaneously improves.

I. Snapper, J. Groen, D Hunter and L J. Witts¹¹² report a series of six cases of an interesting syndrome characterized by achlorhydria, anemia and subacute combined degeneration of the spinal cord in pituitary and gonadal insufficiency The anemia was usually of the macrocytic variety and in two cases responded to liver therapy. It is felt that the anemia had no definite relationship to the endocrinal pathology but was probably secondary to the achlorhydria This conclusion seems unjustified to the RE-VIEWER since anemia and signs of combined system disease are rare in a series of cases of achlorhydria taken at random The endocrinal pathology might have had some direct correlation with the anemia, as has another type of pituitary disturbance (Cushing's syndrome) with the polycythemia which is commonly present

L E Napier¹¹³ describes 11 cases of tropical macrocytic anemia probably due in great part to vitamin B deficiency since they responded to treatment with an autolyzed yeast preparation without added liver F M Hanes and A Mc-Bryde¹¹⁴ discuss a syndrome which has acquired many different names during its "curious history" nontropical sprue, idiopathic steatorrhoea, Gee's disease, coeliac disease The "sprue syndrome" is probably a better name, it has no relation to tropical residence and is probably a deficiency syndrome closely related to tropical sprue Macrocytic anemia is usually present and it is remarkably benefited by adequate liver therapy Macrocytic anemia may also occur in a variety of intestinal conditions as

pointed out by H R. Butt and C H Watkins¹¹⁵ and particularly in disorders of the terminal ilium. Liver extract may be of no value in these cases, which are benefited by surgical procedures. Garnett Cheney¹¹⁶ describes a "megalocytic hypochromic" anemia in pancreatic disease.

K Kato and P E Stemer 117 and E B Astwood^{117a} report cases of aplastic anemia in which the etiologic factor was not discernible although in Kato's case, the child was fond of inhaling the odors of kerosene and gasoline Astwood's case is distinguished by its complete recovery which was apparently consummated by eight transfusions with such supplemental procedures as liver extract, iron, yeast, raw bone-marrow, epinephrine and ephedrine The great majority of the idiopathic cases are fatal, those with a readily discernible etiology (arsenic, arsphenamme, benzol, etc.) stand a fairly good chance for recovery providing supportive measures, chiefly transtusions of blood, are persisted in wood rightly criticizes the concept of complete bone-marrow aplasia as necessary to the diagnosis of aplastic anemia Small islands of hematopoietic tissue may be present and may act as centers of regeneration, thus justifying continued transfusions

Hemolytic Anemias

Many kinds of hemolytic anemia in addition to the well-defined one of congenital hemolytic jaundice are being reported with the result that the literature on this subject is chaotic. This is particularly true of the acute types of hemolytic anemia, which many authors indiscriminately classify under Lederer's anemia. The latter disorder, described some years ago by Max Lederer, is thought to be infectious in origin and characterized by rapidly progressive hemolytic anemia dramatically cured by

transfusion J L Lovibond, 118 among others, reports a case of macrocytic hemolytic anemia in which transfusions were of no value and which was responding to splenectomy until the patient died of sepsis Several similar cases have been reported and the Reviewer has recently seen three more in which dramatic recovery followed splenectomy Is this Lederer's anemia or is it another type? Due to the fact that no sharp dividing lines have been drawn between the various types of acute hemolytic anemia which although superficially similar may be as apart as the poles, cases are being reported under many different headings and doubtless a number of rare, although individually important, cases are not recognized with resultant fatal exitus To miss out on an opportunity for splenectomy in a suitable case may be a fatal error

A few words might be in order regarding the three cases of acute hemolytic anemia which the REVIEWER has seen and which recently have been reported 119 In the first two cases, the blood picture of pernicious anemia was closely simulated but there was no response to large dosage of liver extract Transfusions being of no help, splenectomy was resorted to with dramatic response In the third case, the blood picture resembled that of congenital hemolytic jaundice microcytosis, spherocytosis, increased red cell thickness, very marked reticulocytosis and again there was diamatic response to splenectomy although in each case the patient was in a semimoribund condition In all the cases a unique finding was made hemolysins were discovered which had the faculty of destroying the cells of all the blood groups including those of Group O (Type IV Moss) Numerous experiments demonstrated that this hemolytic factor was probably causally related to the disease and might be produced in the spleen since extracts of the spleen contained large quantities of hemolytic factor. Since the spherocytes in the third case diminished and then disappeared with recovery, the possibility is present that the spherocytosis was brought about by the hemolytic factor. Observations of a similar type in congenital hemolytic anemia have already given suggestive results with the finding of a hemolytic factor there as well. The spherocytes of congenital hemolytic jaundice may thus be the end-result of an hemolysin and not an hereditary factor.

In a fascinating article L P Hamburger and Alan Bernstein¹²⁰ describe an uncommon type of chronic hemolytic anemia associated with paroxysmal hemoglobinuria There was anemia, reticulocytosis and perpetual hemoglobinemia The urine always contained urobilinogen and hemosiderin Transfusion and splenectomy usually did more harm than good A definite group of hemolytic syndromes may be traced from the very severe hemoglobinuria cases (paroxysmal hemoglobinuna—cold—nocturnal) to the mixed cases of hemoglobinuria and hemolytic anemia to acute hemolytic anemia with or without slight hemoglobinuria to congenital hemolytic anemia with or without hemoclastic crises These are discussed by L J Witts¹²¹ and it is possible that hemolysms are a factor in all of them. In the following case reports of Hamburger and Bernstein it may be noted in the text that an hemolysin was once discovered, but was not apparently investigated

Acute hemolytic anemia during therapy with sulfanilamide is being discovered ^{1,2,2} It is apparently similar in type to the hemolytic anemia of phenylhydrazine poisoning and responds readily to withdrawal of the drug T R Waugh^{1,2,3} reports two cases of severe hemolytic

anemia in carcinomatosis with extensive involvement of bone and bone-marrow. These cases are chiefly of interest from the diagnostic viewpoint since occasionally cases of metastatic malignancy and of Hodgkin's disease may present themselves as hemolytic anemia.

R L Haden and F D Evans¹²⁴ report two cases of sickle cell anemia in the white race, both cases responding moderately well to splenectomy patients were sisters born of Sicilian parents-no history or physical finding suggesting an admixture of negro blood These authors suggest that splenectomy should be employed more often in the disease if the spleen is large and the patient seen early in the disease. It is not a cure but only an aid in treatment since W W Cardozo¹²⁵ anemia persists studied the sickling trait in a large number of individuals and found that its inheritance followed the Mendelian law The sickling trait is inherent in the cell and not in the serum and therefore "future investigative attack must be made on the cell itself and not on the serum It may be that the protein constituents of the protoplasmic structure of the cell hold the clue "

Certain Disorders of the Spleen

W P Thompson, J L Caughey, A

() Whipple and L M Rousselot¹²⁶ discuss the splenic vein pressure in congestive splenomegaly (Banti's syndrome)

This syndrome, characterized by anemia, leukopemia, thrombocytopenia and splenomegaly was observed in association with cirrhosis of the liver, partial and progressive obstruction of the splenic vein and in the later stages of schistosomiasis infestation. The conception was elaborated that the common factor in all these cases was portal hypertension. In eight cases accurate pressure readings within the splenic vein were determined.

directly at operation and compared with the pressure within the arm veins Three cases of congenital hemolytic jaundice served as controls These determinations showed extremely high readings in the splenic vein (275, 325, 450, 275, 470) as compared to the arm vein (12, 85, 125, 105, 140) and certainly suggest, as the authors state, that portal hypertension may be an important factor in the production of chronic splenomegaly. From the same "Spleen Clinic," A. O Whipple127 describe the organization of such a group and its value in study of patients and in teaching and research. The operative results of splenectomy are recorded in the various types of spleen disease The poorest results were obtained in Laennee's cirrhosis of 15 cases of pretty typical Banti's syndrome, the results have been good in two-thirds of the cases Hematemesis in these cases is of very grave prognostic import, and it is felt that operation is of no value when hematemesis has occurred

In a symposium on certain rare disorders of the spleen in the Journal of Pathology and Bacteriology (British), careful descriptions are given of unusual syndromes Norah H Schuster¹²⁸ describes a case of familial hemorrhagic telangiectasia associated with multiple ancurisms of the splenic afterv. H. A. Magnus¹²⁹ described two cases of multiple necrosis of the spleen ("speckled spleen") which may be due to arteriosclerotic, toxic, thrombotic or arthritic causes (r R Tudhope¹³⁰ reports a case of splenomegaly with "inveloid transformation" There are said to be no features in the blood suggestive of leukemia, although the marked anemia and leukocytosis are suggestive Most of the marrow was fibrotic but active proliferation was seen in several areas. This case was probably one of aleukemic myelogenous leukemia with a very large spleen as the outstanding feature These cases are not unusually rare and it is safe to state that many a spleen has been removed for "splenic anemia" when the diagnosis has in reality been chronic aleukemic myelogenous leukemia.

Polycythemia

The etiology of the "true" or "primary" type of polycythemia is still an unsolved riddle, although most observers have the "hunch" that an anoxemic condition of the marrow is probably present An attempt to bolster this conception is the work of Reznikoff and collaborators already referred to in last year's review and indicating that the blood vessels of the marrow showed evidence of disease From the experimental standpoint, it is difficult if not impossible to interfere with the circulation of such a widely scattered organ as the marrow and from the clinical standpoint, it must be admitted that only an occasional marrow in polycythemia will show the welldefined changes pictured by Reznikoff and collaborators The theory that the disease is due to a hypersecretion of "addisin" and therefore the antithesis of pernicious anemia (Morris and collaborators) has been pretty well discredited About a quarter of the Reviewer's cases of polycythemia present achlorhydria and in most the free acid is present in normal or somewhat diminished quantity Peptic (gastric or duodenal) ulcer is present not infrequently—in 4 or 25 cases observed at the Beth Israel Hospital. Manfred Kraemer and Maurice Asher¹³¹ report two cases in which duodenal ulcer and erythrenia were coexistent and refer to the report of D L Wilbur and H C Ochsner¹³² who found that eight per cent of the 143 cases of polycythemia at the Mayo Clinic presented peptic ulcer. Kraemer and Asher attempted to reduce the red cell count in one of the above two cases by daily gastric lavage. The patient's ulcer symptoms were relieved but his red cell count showed no change and the therapy was discontinued The most important etiological factor seems to be racial, as observed by Reznikoff. Twentyfour of our 25 patients were Jewish, most of them Russian or Polish in origin. Statistics from many clinics show that polycythemic patients are usually Jewish, although the Jewish group may number only about ten per cent of the hospital population The occurrence of polycythemia in various neurological and endocrinological conditions is well known and has been the occasion for suspecting a neuro-endocrine stimulus of erythropoietic activity as well as considering that the etiology of polycythemia is to be found fundamentally in the same cerebral A Ferraro and W. D. Shercenter wood133 discuss these views in describing the coexistence of polycythemia with chronic encephalitis and paralysis agitans Two cases with definite polycythemia are reported and the literature relating to the coexistence of the two conditions Polycythemia is thoroughly reviewed has been described in association with lesions of the basal ganglia, the adrenals and the pituitary Involvement of mesodiencephalic centers is thought to be related to the development of polycythemia vera

Certain cases of polycythemia with known etiology are of interest, particularly those in which pulmonary arteriosclerosis is present ("Ayerza's disease") Ward Darley and C A Doan¹³⁴ report a well studied case of this sort in which there was extensive pulmonary arteriolar sclerosis with dilatation of the pulmonary artery and right ventricular hypertrophy. The red cell count was about 7.5 million and the total blood volume was increased

In our experience, the diagnosis of polycythemia is frequently missed, and

the patient may go about for several vears labelled as heart disease, vascular disease of the extremities, migraine, etc. The vascular complications of polycythemia are reviewed by I L. Norman and E. V. Allen 135 In 98 cases observed at the Mayo Clinic, vascular complications occured in 33, intra-abdominal thrombosis. six: coronary disease, five, cerebral vascular disease, six; peripheral occlusive vascular disease, seven, erythromelalgia and burning paresthesia. eight, vasospastic phenomena, one. It is important to be on guard for possible polycythemia in the presence of various vascular disorders, particularly of the The diagnosis should be extremities considered in all individuals with a plethoric appearance, particularly if they are of Jewish origin Other important points in the physical examination are the condition of the fundus oculi and the The retinal question of splenomegaly veins show marked distention and appear intensely blue The retinal arteries are normal in the "primary" type, according to Martin Cohen 136 and congested in the "secondary" types spleen, which is extremely variable in both position and size, was felt in 15 of the Reviewer's 20 cases. It may not be felt, even in some of the most severe cases A hemoglobin test (by the commonly used Tallqvist method) is of no value and so a red cell count should be done in suspected instances It might be well to perform a red count in all cases of vascular disease of the extremities. the occasional instance of the disease discovered in this manner more than compensates for the many normal counts

Treatment of the condition is still unsettled, some observers continuing to recommend *phenylhydrazine*, others *x-ray therapy*, and others — more recently—frequent *venesections*. Phenyl-

hydrazine is a difficult drug to control, requiring much co-operation on the part of the patient X-ray therapy is expensive, drastic, and almost always unsuccessful in the Reviewer's experience F T Hunter¹³⁷ reports excellent results with "spray" radiation in two cases of the disease We have been unable to affect the disease at all in three cases using the similar small dosage in "spray" form as recommended by Hunter Our chief reliance in recent years has been in the production of an "iron-deficiency state." This consists in the removal of 500 cc of blood twice weekly for three to four weeks at the beginning of treatment, followed by the induction of a diet deficient in iron. With this method, the patient's symptoms completely clear up, the hemoglobin is kept between 75 and 85 per cent of normal, and the erythrocyte count between 50 and 70 nullion. The hematocrit and hemoglobin are the important things to watch, and these generally remain at normal or slightly low levels for six to nine months, following which another small series of venesections is given. (The venesected blood is used for transfusion purposes.) The method has proved very successful m ten successive patients and is entirely tree of the dangers of phenylhydrazme toxicity and of drastic roentgen-ray ther-It is furthermore physiologically sound Very similar therapeutic results have been obtained by D. J. Stephens and N. L. Kaltreider¹³⁸ in four of five cases. An non-deficiency diet was apparently not used

Disorders of the White Blood Cells

Glandular Fever—Last year's statement in this review that glandular fever is one of the most commonly overlooked diseases in general practice does not, unfortunately, require modification at this time. I Davidsohn¹³⁹ points out the

many conditions with which the disease is often confused "Grippe" is of course the most obvious the patient has a sore throat, slight fever, and the lymphadenopathy is not suspected. Since abdominal pain is present in some 20 per cent of the cases due to involvement of mesenteric lymph-nodes, the diagnosis of appendicitis may be made and the patient operated upon Furthermore, since the leukocyte count is commonly elevated, and a differential count is rarely done, it is readily seen how the error may be made Some of the cases of so-called mesenteric adenitis are in reality examples of the more generalized disorder "infectious mononucleosis" I have seen cases of "catarrhal jaundice," "purpura," "streptococci sore throat" turn out to be typical examples of the disease, once the lymphadenopathy and the blood picture were recognized More care in the palpation of lymph-nodes in their respective situations would result in the presumptive clinical diagnosis of the disease, the final diagnosis then being made from examination of the blood smear and by performance of the heterophile agglutination test

The pathology of the lymph-node has not been studied very extensively, although recently it has been put on a firmer basis by the publication of H Downey and J Stasney 140 These observers point out that although occasionally the node resembles the picture of leukemia, there is never the complete loss of structure seen in advanced cases of leukenna and no invasion of the capsule The reticulum is generally hyperplastic with transformation of some of the cells to lymphocytes The blood picture is the end result of the extreme hyperplasia found in the lymph-nodes and indicates "a reaction that is more or less leukemoid in nature to an infective, toxic, lymphotrophic agent"

The nature of the infectious agent has not vet been elucidated. What relation it has to the positive sheep cell agglutination test has vet to be worked out Studies continue to be made on this most interesting diagnostic test which so far has been shown to be positive only in serum sickness and infectious mononucleosis. The work of several groups of investigators indicates that the agglutinins of serum sickness are of a different type than those of glandular fever and may thus be appropriately absorbed on testing Peter Beer¹⁴¹ contributes an important article in which stress is placed upon the differential testing of suspected blood serum with the cells from horses. goats, cows, as well as sheep. Methods are outlined for differentiating cases of serum sickness from infectious mononucleosis

Although it is comforting to obtain a positive agglutination test, the diagnosis should readily be made from the blood picture which shows (1) marked lymphocytosis. (2) extreme variability in the types of lymphocytes with all sorts of large, abnormally shaped and abnormally stained cells, (3) no anemia, and (4) no reduction in blood platelets. The latter three criteria are of importance in distinguishing the condition from acute leukenna which shows (1) monotony of leukocytic picture, (2) anemia, (3) reduction in blood platelets. In many mild cases the heterophile test is negative N Rosenthal (personal communication) tells me that the test is positive in only about 30 per cent of his cases Complications are rare. High fever may at times be present, this is usually in association with secondary involvement of glands with Vincent's infection In these cases the intravenous injection of neoarsphenamine in small doses trequently results in dramatic drop in temperature and reduction in size of the glands. Otherwise, no treatment is necessary in the disease and all patients make an uneventful recovery.

Agranulocytosis-In last year's review, a fairly complete summary of the present status of the disease agranulocytosis was presented. The disease seems to be becoming less common Whether this is due to the lessened ingestion of amidopyrine and dinitrophenol cannot be stated. The definite impression has been obtained from study of these cases that the bone-marrow, in common with other organs, can be involved in the Amidopyrine has allergic reactions been shown by W. Dameshek and A. Colmes¹⁴² to be definitely toxic to the marrow in the hypersensitive individual. One-twelfth of a grain introduced intradermally was sufficient to induce a typical attack of the disease in two of four individuals. Positive skin tests were obtained in all four cases by the use of a special technic in which the drug was "aged" with blood scrum. The bonemarrow is apparently involved, the marrow leukocytes prevented from maturing, the blood thus becoming depleted of mature granulocytes, and the normal cellular defenses thereby suffering "angina," high fever, etc., are in all probability simply evidences of secondary infection due to organisms which have been able to multiply in the absence of granulocytes. The treatment is based upon an attempt to stimulate the processes of maturation. This is done by the use of the pentose neucleotides ("pentnucleotide") or by the more active adenine sulfate, the latter given intravenously. It diagnosis is correct and made early, treatment should be effective If the diagnosis is incorrect (agranulocytosis secondary to aplastic anemia or leukemia) or if the condition is unrecognized until patient is completely moribund, treatment is without effect

Leukoses (Leukemia) - Since the time of Virchow, who first described in 1847 a case of "weisses Blut," the only progress which has been made in this disease has been in the fields of classification and description Most authorities are agreed upon the malignant neoplastic character of the disease, although an occasional observer discusses the possible infectious or metabolic character of the disease. B K Wiseman¹⁴³ in a lengthy and important paper, discusses the possible "metabolic" character of certain cases of leukenna from a clinical analysis of various types of lymphoid hyperplasia After a discussion of normal lymphopoiesis, Wiseman takes up the history of the development of our concepts of the lymphoid hyperplasia and divides them into four main types lymphatic leukemia, lymphatic pseudoteukemia, leukosarcoma, and aleukocythemic (aleukemic) lymphatic leukemia "Lymphatic pseudoleukemia" is the same pathologically as lymphatic leukemia except that the cells do not get out into the blood-stream (are "screened out"?) Leukosarcoma represents a sarcomatous disorder of lymphoid tissue with the formation of pathological lymphocytes which get out into the blood-stream and give the picture of leukenna. Meukocythemic (alcukemic) lymphatic leukemia is a disorder in which the cells are lost from the blood-stream into the tissue spaces and tend to overgrow the blood-forming organs. Wiseman concludes that there are two types of lymphatic leukemia (1) a metabolic form which is probably more common and in which the cells are normal in type, but which do not mature as they normally should, and (2) a neoplastic form which tends to overrun tissues in typical malignant form The concepts of Wiseman are based on much study and observation and al-

though in many respects unorthodox are worthy of careful consideration

In last year's review, the experimental observations of Furth were discussed These concerned the transmission of leukemia from rat to rat with the production of local neoplasms, leukemia, and aleukemic states at will according to the method of injection utilized Not infrequently one sees clinically sarcoma (either myelosarcoma, lymphosarcoma, reticulum-cell sarcoma) with primitive cells in the blood smear corresponding to the type of tumor This occurs not infrequently in "multiple myeloma" which in reality is a tumor of plasma cells Plasma cell leukemia is occasionally described as in recent reports by A J Patek, Jr, and W B Castle,144 A Jores and W Bruns,145 and H Fleischhacker and R Klima 146 The difference from the pathologist's standpoint between a local tumor composed of blood cells and the diffuse process called leukemia is often indistinguishable "Leukemia" is thus in reality a clinical diagnosis which may indicate a local tumor with metastasizing cells in the blood or a generalized disease without local fumors

C E Forkner¹⁴⁷ reviews and discusses "the confusion existing in the classification and terminology of diseases of the blood-forming organs, particularly of leukemia and related disorders" This confusion is dispelled, according to Forkner, by "a classification which encompasses all known variants of leukemia and which simplifies the concepts of these disorders" Forkner decries the tendency in recent years for the substitution of newer terms for "older equivalents" He then introduces several new terms of his own, viz, "neutrofilocytic leukemia" (instead of "myelogenous leukemia") He complains that certain authors such as Osgood and the Re-VIEWER have confused the issue in regard to monocytic leukemia and the origin of the monocytes, that there is no justification for the terms reticulo-endotheliosis or reticulosis: that there exists "no clear-cut evidence to indicate that monocutes are related in any intimate way with the reticulo-endothelial system considered in its strict sense" The multitude of really authoritative investigations directly contradictory to Forkner's views are not mentioned by this author Suffice it to say that they represent the great majority of present day opinion Forkner brings order out of chaos with his table of classification (This is similar in many respects to that proposed by the Reviewer several years ago (cf previous reviews) and by Callendar in his semiofficial registry of leukemias)

Instead of the paradoxical term "aleukemia leukemia," P Emile-Weil, P Isch-Wall and S. Perles 148 suggest the term "cryptoleukemia," which they feel can often be diagnosed by splenic puncture Although the latter is doubtless quite a simple procedure, the REVIEWER has hesitated to adopt this test and has instead carried out sternal bone-marrow biopsy. In various disorders in which the spleen is involved, much can be learned from study of the marrow Many case reports of monocytic leukemia continue to be published of the best of these with careful descriptions of the postmortem findmgs and blood picture (good colored plate) is that of K Kato 149 R R Kracke and Hortense Garver¹⁵⁰ make some important observations on the diagnosis of leukemia in which the recommendation is made that the physician and not the technician be responsible for the diagnosis The Reviewer can confirm Kracke's experience that the primitive cells-histiocytes, myeloblasts, lymphoblasts-of acute leukemia are more often than not called "large mononuclears" or "large lymphocytes" and thus their diagnostic significance not realized. This happens more often with slide smears which are frequently too thick for careful study of individual cells than with smears made with cover slips. In cases of leukemia with normal or low leukocyte counts, study of the "buffy coat" of the blood after it has been centrifuged may reveal many primitive cells difficult to find otherwise H. Keilhack¹⁵¹ reports an interesting case of chronic aleukemic myelosis with hyperproteinemia High blood proteins have heretofore been reported, aside from Kala-azar, only in association with plasma cell tumors ("multiple myeloma") Keilhack's report in which the total protein was 743, albumin 180 and globulin 516 is the first showing increased globulins in inveloid leukemia There is a possibility, however, that the diagnosis was not correct since the lymph-nodes were greatly enlarged, a very unusual finding in myeloid leukemia S M Goldhamer and B Barney¹⁵² report a case of myelogenous leukemia with cutaneous involvement, which is rare in this disease, although much more common in the chronic lymphoid type (A generalized macular infiltrative eruption is seen commonly m acute monocytic leukemia)

A case of lymphatic leukemia in which the only gross manifestations were in the breasts is reported by B. Joan Haram ¹⁵³ First one breast, then the other became involved by tumor. The blood, at first negative, then showed the typical findings of lymphatic leukemia. The breast tumor was histologically sarcoma. This case illustrates that leukemia may be secondary to lymphosarcoma and not the primary disturbance.

The same statement holds true for the so-called "leukemia cutis" which consists of lymphomatous nodules which may sooner or later show changes in the blood typical of leukemia. A case of this type is reported by J. M. Hitch and D. C. Smith 154.

Monocytic leukemia continues to be reported in ever increasing numbers Thus E E Osgood¹⁵⁵ describes six new cases with reports of 147 other cases This form of cited from the literature leukemia seems to be about as common as its recognition. The most characteristic clinical features are the very acute course, the unusual tendency to swelling of the gums, and the frequent association of fever, stomatitis and hemorrhages Osgood comments on the bone-marrow (puncture) findings in the disease and attempts to make sharp differentiating features between monoblasts, promonocytes, and monocytes. He concludes that the mature monocyte arises from the monoblast in the marrow and develops through the stage of the promonocyte into the mature monocyte of the normal blood Hamilton Montgomery and C. H. Watkins 156 state that it is important to distinguish between the so-called Naegeli type of monocytic leukemia and the true Schilling type (leukemic reticulo-endotheliosis) However, in a revealing sentence, they state, "For this reason it is probable that the Naegeli type of monocytic leukemia is a form of invelogenous leukemia and not a distinct entity" (!!) If this be the case, why include these cases of inveloid leukemia with atypical myeloblasts in the group of cases of monocytic leukemia? The latter is, as these authors point out, a distinct entity, the primitive or type cell being the reticulo-endothelial cell Monocytic leukemia should be regarded as a distinct entity, to divide it up into subtypes is unwise, myeloid leukemia is myeloid leu-

kemia and not the Naegeli type of monocytic leukemia. Naegeli has continued to resist the concept of this third form of leukemia. To name a myeloid form of monocytic leukemia for this author is therefore poor compromise.

H Penzold¹⁵⁷ contributes a very able discussion on "reticulosis as a system disorder of the reticulo-endothelial apparatus" The case report is similar in most respects to that reported by the Reviewer some years ago as "aleukemic reticulosis" This disorder is a generalized ("leukemic") one, being related to the local reticulum-cell sarcoma as lymphatic leukemia is related to lymphosarcoma Penzold agrees with the classification of reticulo-endothelial disorders of other authors, which is as follows

- 1 Storage disorders (Gaucher, Niemann-Pick, etc.)
 - 2 Acute reticulo-endothelioses
- 3 Generalized reticulosis, a system disorder
- 4 Reticulum cell sarcoma, a local disorder

Although Penzold agrees that the subject of the monocyte, reticulosis, etc, is still in a more or less confused form because of the absence of known etiological factors, his objective analyses are refreshing after a reading of Forkner's dogmas, referred to above

Lymphatic leukemia in association with pertussis is reported by Walter Levy, M. J. H. Grand, and S. A. Krakauer ¹⁵⁸. The difficulty in differentiating one condition from the other is emphasized, particularly in those cases of pertussis with extremely high leukocyte counts, which should be carefully followed up. A. A. Holbrook ¹⁵⁹ reports a case in which chicken-pox and lymphatic leukemia were coexistent. Holbrook feels that although the conditions were simultaneously present, they were entirely coincidental, the chicken-pox, how-

ever, probably modified the leukemia so as to cause marked dermatological localization; and *vice versa*, the leukemia probably modified the course of the chicken-pox

The treatment of leukemia remains as discouraging as ever The acute types are better given large doses of sedatives and thus made relatively comfortable Transfusions, x-ray therapy, and liver often may distress the patient without modifying his disease in the slightest X-ray treatment in the chronic cases should be given only when it seems essential for the relief of symptoms have often seen a relatively healthy patient become bedridden because of too meddlesome therapeutics in this direction. Too often the blood count and not the patient is treated X-ray therapy, judiciously handled by the radiologist in close collaboration with the internist, is often of great value "Spray" treatment or total roentgen therapy seems to be the present method of choice of many radiologists. It is useful, as I. Belot¹⁶⁰ points out in disorders which involve the entire organism and therefore in leukemia. In the REVIEWER'S experience, "spray" treatment has been disappointing. H. F. Lucdman (personal communication) obruns better results with the use of intensive local dosage given in turn to various neas of the body, the whole body gradually being covered. D. J. Stephens and 1 > Latwicince 161 report on their experience with Fowler's solution in the treatment of chronic inveloid leukenia They recommend it as an effective palliative agent, comparing favorably with x-ray therapy. It may perhaps be used most advantageously in conjunction with or alternating with irradiation x-ray therapy is not readily available. the drug may well be used, although its effects on the platelets are often disas-The REVIEWER has discarded its

use because of the frequency of toxic effects. D. I. Stephens¹⁶² describes the bone-marrow picture at biopsy from two cases of chronic myelogenous leukemia before and after therapy with Fowler's solution and roentgen therapy. In each instance the gray, hyperplastic, cellular leukemic bone-marrow was replaced by a relatively hypocellular, fibrotic marrow and the markedly increased myeloiderythroid ratio was decreased to an approximately normal level W S Middleton, O. O. Meyer, and E. A. Pohle¹⁶³ give their experience with radiotherapy in leukemia with particular reference to the effect on the basal metabolic rate The metabolism which is commonly elevated in chronic lymphoid leukemia may act as one of the guides in further therapy. The authors stress the necessity for individualization of therapy

Tumors of the White Cells

E B Krumbhaar, 164 for want of a better term,* proposes that a host of conditions widely dissimilar in morphology, ctiology, and in many other ways, be called the "lymphomatoid diseases" Even a large and loosely-constructed waste basket would not be expected to hold very comfortably the variety of conditions which Krumbhaar has assembled. The various leukemias, the various sarcomas, mycosis tungoides, Hodgkin's disease, agranulocytosis, Cooley's anemia, infectious hemolytic anemia, hepatic thrombosis and von laksch disease. This article deserves careful reading, however, because with Dr. Krumbhaar's wide experience many apparently unrelated conditions are brought together and discussed in a manner both philosophical and profitable. His classification of 'primyclogenous, lymphocytic mary

^{*}He does not like the terms commonly used in Boston of lymphoblastoma" and "malignant lymphoma"

reticular disorders" is quite in keeping with the classifications which have been offered in these reviews in the past two years. Thus there are three blood-forming tissues: Bone-marrow, lymphoid tissue, and reticulo-endothelial system All of them may be subject to generalized (leukemic), localized (sarcomatous), leukemic or aleukemic processes, or to combinations of these. This sort of classification is more in line with the statement which Krumbhaar quotes James Ewing as making in 1927, "Although we may not be able to find clear differences in all cases, how are we going to make progress by throwing them all into one category? I would rather see the most minute differences emphasized and a classification based upon these until the time when the etiologic factors unify or subdivide the entire group" For the tumors of the blood cells, as simple a classification as any is that given in last This may be repeated year's review he re

kemia is simply a metastatic feature in the blood of chloramatous myeloblasts. The same situation is occasionally seen in lymphosarcoma and plasmacytoma when, during the course of the proliferation, lymphoblasts and plasma cells respectively appear in the blood in large numbers. Myeloid leukemia and chloroma are therefore probably different manifestations of myeloblastic proliferation

H M Ewing and M J Fein¹⁶⁶ report a case of "follicular lymphoblastoma" which is characterized by generalized lymph-node enlargement and splenomegaly and pathologically by the presence of extremely large (giant) follicles. This condition is apparently malignant, and related to benigh hyperplasia on the one hand and to lymphosarcoma and lymphatic leukemia on the other hand. It is radiosensitive, chronic in its course, and frequently accompanied by the blood picture of chronic lymphatic leukemia.

Henry Jackson, Jr, Frederick Parker, Jr, and A M Brues¹⁶⁷ describe under

Tissue
Bone-marrow
Lymphoid tissue

Highly Malignant Myelosarcoma (chloroma) Lymphosarcoma Less Malignant

Myeloma (not "multiple myeloma")

Lymphoma

Plasmacytoma ("multiple myeloma")

Reticulo-endothelioma

Reticulo-endothelium Reticulum-cell sarcoma Hodgkin's disease

Ernestine V Kandel¹⁶⁵ gives a comprehensive review of chloroma and adds 40 very carefully selected cases to the 129 already reported. The green pigment of the tumor is apparently a lipochrome which may contain iron. Decolorization takes place upon exposure to air but the color returns when the tissue is soaked in a solution of hydrogen peroxide. Since cases are always associated with myelogenous leukemia, Kandel concludes that "chloroma is simply a variant of myeloid leukemia." The Reviewer would rather conclude that the blood picture in acute myelogenous leu-

the "Boston" term of "malignant lymphoma" of the tonsil, 37 cases including reticulum-cell sarcoma, lymphocytoma, Hodgkin's disease, lymphosarcoma, giant follicle lymphoma and plasmacytoma. The progress of these cases is extremely variable and unpredictable although practically always downhill to death. The number of mitoses per oil-immersion field gave, in a general way, some indication of the progress. Thus, those with ten mitoses per oil-immersion field were fatal in less than six months; those with but one mitosis or less caused death in three years or over. The authors warn

against the deceptive character of the initial radiosensitivity to x-ray therapy

Hodgkin's Disease

The tendency more and more is to group this disease among the proliferative lesions of the reticulo-endothelial Although the disease usually originates in the lymph-nodes, it is not necessarily a disorder of lymphoid tissue ter se, since the lymph-nodes contain two widely different types of cells. Lymphocytes and reticulum cells The latter cells differ histologically and functionally from the lymphocytes and make up, together with similar cells in the bonemarrow, the liver, and the spleen, the reticulo-endothelial system. The reticulum production in Hodgkin's disease, and the formation of giant cells are quite characteristic of reticulum cell rather than lymphocytic proliferation. On the other hand, Medlar interprets the disease as being due to a hyperplasia of megakarvocytes, bone-marrow cells which have migrated to lymphoid and other tissue and have proliferated there. Medlar feels that megakaryocytes in the peripheral blood are frequently unrecognized and are often confused with monoeytes 168. However, he admits that it is often difficult if not impossible, to ditferentiate definitely between one cell and the other. Medlar has studied the subject of possible megakarvocytic hyperplasia very carefully and although his views are directly contrary to the opinions of practically all other investigators, they cannot be completely disregarded

Several groups of investigators 109 170 171 172 report their results with the Gordon test in Hodgkin's disease. The test consists briefly in the injection of an emulsion of the suspected lymph-node into the brain of rabbits. In a positive reaction, the rabbit develops various types of cerebral reactions such as ataxia, spasticity, and convulsions. Friedemann in 1934 reported that this test could be obtained with normal bonemarrow Until very recently, the pathogenesis of the test had been unknown. However, in May, 1937, J. C. Turner and Henry Jackson, Jr. 173 showed quite conclusively that the reaction is specific only in so far as the eosinophile is concerned and will be positive only when eosinophilia is present Eosmophilia from a variety of conditions will produce the same kind of paralytic action in rabbits. This explains why normal bonemarrow with its content of eosmophiles gives a positive test and why the fibrotic lymph-node of Hodgkin's disease, without eosinophiles, gives a negative re-P Emile-Weil, P. Isch-Wall. and S Perlès¹⁷⁴ recommend the technic of lymph-node puncture which they have used with excellent diagnostic results in In each instance they con-20 cases trolled their observations with actual biopsy. The principal diagnostic criteria in the puncture material were endothelial elements and authentic giant cells of Steinberg The REVIEWER can confirm the simplicity and accuracy of this simple procedure, which might well be generally adopted, although for the first year or so it should always be checked with actual biopsy removal of a node. The method consists in puncturing an accessible lymph node with an 18 or 20 gauge needle and drawing up a very small amount of material into the needle by the use of suction from a 20 cc syringe. The resultant bits of material are smeared on glass slides which are stained with Wright's or Giemsa stain. Our attention was first drawn to this method by Alfred Paylovsky of Buenos Aires, Argentina,175 who has written a monograph on the subject. For simple bedside differential diagnosis between lymphosarcoma, Hodgkın's disease, tuberculous adenitis, and

infectious adenitis the method may be invaluable.

Grace M Roth and C H Watkins¹⁷⁶ point out from a study of 40 cases that there is no specific morphologic blood picture diagnostic of Hodgkin's disease This is quite true, and is also referred to in the article of Medlar and collaborators referred to above "Typical" blood pictures are seen only when one knows the diagnosis in advance. Very little new regarding either the diagnosis, pathology, or treatment of the disease has been written An interesting paper is contributed by Katrine Ebbehøj,177who describes minutes the findings in 44 verified cases In the lungs the disorder may be confused with tuberculosis. The bony system may be involved, generally in the second year of the disease, bony defects are generally the rule, although osteoblastic and sclerosing torms are also found H W Jacox, C B Peirce and R (Hildreth 178 report on the treatment on 161 cases within the past decade Definite extension of life was induced, as compared with untreated patients, systemic (spray) irradiation was of no greater effect than repeated local treatment, future figures with treatment may be better because of improved and more intensive methods of therapy

The Hemorrhagic Disorders

Disturbances of the Coagulation Mechanism - Harry Fagle 179 contributes an important review on the "blood coagulation problem" in which are discussed the various theories of blood coagulation, together with a summary of Eagle's recent work. This has demonstrated that trypsin or certain snake venoms can activate profitionibin to thrombin in the absence of platelets and calcium. It is probable that calcium and platelets together constitute a proteolytic enzyme analogous to trypsin

Another enzyme reaction then occurs that between thrombin and fibrinogen to form fibrin Certain proteolytic snake venoms can also accomplish the same procedure Why circulating red cells do not clot is as yet unknown Apparently plasma has an antithrombic action No definite statement can be made as to coagulation defect in hemophilia although it probably centers about the prothrombin-thrombin combination The same holds true in jaundice. In another paper, the same author 180 details his experiments on the coagulation of blood by snake venoms and discusses their physiologic significance Certain venoms act directly on fibrinogen converting it to fibrin, whereas others act on prothrombin to form thrombin Extraordinarily minute quantities of some of these venoms sufficed to produce a demonstrable activation to prothrombin Thus the fer-de-lance (Bothrops atrox) venom was active in a 1 25,000,000 dilution, and that of the Australian tiger snake in a 1 4,000,000 dilution. The coagulation phenomenon, Eagle concludes, is the result of two consecutive enzyme reactions (1) the conversion of prothrombin to thrombin by either calcium and platelets, or by trypsin and proteolytic snake venoms, (2) the conversion of fibrinogen to fibrin by either thrombin, papain, or proteolytic snake venoms A I Patek, Ir, and F H L Taylor¹⁸¹ continue their investigations on the coagulation defect in hemophilia. As noted in our pictious review, these have already shown that the clot-promoting substance absent in hemophilia was associated with a saline soluble globulin This was thermolabile fraction hemophilia, there must be a specific alteration in the "prothrombin complex"; although it is present in the globulin fraction of the serum, there is no proof that it is globulin itself. It may be of enzymatic nature. The clotting time of hemophiliac blood may be reduced in 2120 by injecting "globulin" substance. Since this substance may be dried and powdered, future investigations may result in the production of an extract to keep the coagulation time of hemophiliacs to within fairly normal limits. This substance is as vet not available F J Pohle and F H L Taylor¹⁸² continue investigations on the effect of intramuscular administration of globulin substance in hemophilia and report a definite diminution in coagulation time which lasts for 24 hours and is then followed by a refractory phase R C Eley¹⁵³ describes his experiences with the extract of normal human placenta in the treatment of hemophilia (These results may not in children apply to adults). Of 19 children receiving placental extract, 12 developed a reduction in the coagulation time to nor-The material is given inmal limits tramuscularly and may even be taken by mouth

Purpura - This may be associated with a reduction in platelets or with vascular changes. In last year's review, a tanly complete review of the problem was present and this may be consulted I M Tocantins 184 presents a critical review of the various technical methods for the study of blood platelets should be consulted by those who are interested in studying these somewhat reglected bodies. Thrombocytopenic pinpura due to food allergy is described by I L Squier and F W Madison 185 The same procedure was used with foods and the study of the platelets as with the determination of the leukopenic index Thrombocyte depression after ingestion of specific foods was observed in two cases of thrombocytopenic pur-The authors are "convinced" of the importance of an allergic factor in

many of the cases of purpura (whether thrombocytopenic or "anaphylactoid") The Reviewer feels very skeptical about this demonstration: (1) Platelet counts fluctuate widely, (2) the method used is relatively inaccurate, (3) remissions or relapses in thrombocytopenia are notoriously common and all conclusions regarding the therapeutic effect of various measures must be guarded. S. R. Mettier and Katharine Purviance¹⁸⁶ present a classification of hemorrhagic discusses which seems logical and adequate for present needs. In condensed form, this follows:

- I Deficiency in blood-clotting elements
 - 1 Thrombocytopenic purpura—essential or idiopathic, symptomatic (bone-marrow destruction).
 - R Fibrinogen-liver disease
 - C Calcium
- II Ibnormality in blood-clotting elements
 - 4 Obstructive jaundice
 - B Hemophilia
- III Defect in Vascular Mechanism
 - 1 Allergy
 - B Nutrition-scurvy
 - C Infectious diseases
 - 11 Arteriosclerosis
 - E Toxic (snake venom, etc.)
 - F (ongenital (hereditary hemorrhagic telangiculasia)

S. M. Peck, N. Rosenthal, and Lowell \ Frf187 present a comprehensive review (with emphasis on the dermatolog ical viewpoints of purpura. Purpuric manifestations may be petechiae, ecclivmoses hematomata, vibices (linear ecclivmoses), and suffusions. The red color of petechae is due to the presence of small dilated vessels filled with blood and of a small amount of hemorrhage immediately below the epidermis or in the upper lavers of the cutis dilated vessels and free hemorrhage, a bluish lesion was present. Purpuric hemorrhages are the result of blood escaping from the "minute vessels" of the skin (diapedesis or actual vessel rupture)

The intradermal venom test may be utilized for testing the capillary permeability This is performed by the injection of 01 to 02 cc of moccasin snake venom (Lederle) intradermally (salt solution control). A positive reaction is a definite hemorrhage 1 cm or more in diameter appearing at the site of injection, reading is usually made at one hour, although delayed reactions may take place Skin biopsies were studied histologically from purpura produced experimentally in normals and in cases of thrombocytopenic purpura both by suction (diapedesis) and by snake venom (rhexis) and in various disease states associated with purpura. It was found that the elastic tissue in the cutis played an important role in the mechanism of purpura, acting as a 'shock absorber" in the prevention of undue stress and strain on blood vessels. With loss of elastic tissue and resultant weakening of vessel walls, purpuric manifestations might occur The authors then describe their technic and experiences with the use of moccasin snake venom therapy A positive reaction to venom usually indicated the need for venom therapy. The material was given subcutaneously in increasing dosage beginning with 0.4 cc and given every few days, unless bleeding was brisk, when it was given daily When sensitivity developed, desensitization was employed. The venom probably acts on vessel walls, making them resistant to hemorrhage. The REVIEWER has seen no benefit result from this form of therapy in cases of thrombocytopenic purpura, although its value in hereditary hemorrhagic telangiectasia and in vascu-M A Goldlar purpura is possible berger and S M Peck188 report good results in 17 of 20 cases of functional uterine bleeding Very little effect on uterine bleeding due to fibromyomas was noted.

R B. MacFarlane¹⁸⁹ recommends the use of Russel's viper venom for application locally to stop bleeding in cases of hemophilia This venom was obtained from vipers in the collection of the Zoological Society of London and was effective in clotting hemophilic blood in a concentration of one in one billion within six minutes. It was used locally on external wounds or to the gums after dental extractions with success in five of B Barnett¹⁹⁰ reported seven cases similar results with the same venom applied locally in six cases of hemo-These results are similar to philia those obtained by S Rosenfeld and S E Lenke,191 who used the venom of the Australian tiger-snake which readily clots 12,800,000 times its weight of heavily citrated or oxalated blood These authors find that tiger-snake venom is superior to Russel viper venom in many important respects W A Timperley, A E Naish, and C A Clark¹⁹² report the discovery of a nonprotein substance derived from egg white which when given intravenously to cases of hemophilia shortened the clotting time and stopped further progress of symptoms

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DISEASES OF THE KIDNEY

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INTRODUCTION

Although there have been no epochmaking advances this year in the diagnosis and treatment of diseases of the kidney, numerous important articles have

appeared in the literature which tend to give a clearer conception of the relationship of clinical phases of renal disorders to the fundamental derangements of the physiology and pathology of the kidney

Each year the etiological factors of nephritis are becoming better recognized and the clinical diagnosis more exact. This year's literature is richer in articles on treatment than that of last year, but pathology and diagnosis appear to be the subjects of chief concern. In this review, as in those of other years, articles on all phases of *Bright's disease* will be reviewed, but more emphasis than usual will be given to those articles dealing with treatment of renal disorders.

ACUTE NEPHRITIS

Much has been written during the past year on the importance of early diagnosis and proper treatment of acute nethritis in reducing the incidence of the chronic form which caused 92,272 deaths in the United States during 1935 When we consider this, and realize that, once chronic nephritis has set in, the outlook is grave, the necessity of preventing its development is clearly apparent. It has been emphasized also that acute nephritis frequently follows upper respiratory infections and that urmalysis is of great importance in the discovery and adequate treatment of the early mild cases significance of acute glomerulonephritis in childhood has been a subject of contioversy for years. If the disease runs a definite course with a low mortality and consistently goes on to complete recovery as many observers contend, it is of little significance, but, on the other hand, if the acute nephritis of childhood is connected directly or indirectly with the various types of chronic nephritis of later life, then its diagnosis and treatment are highly important

Bierman¹ followed 35 cases of *acute* nephritis in children from one to five years. Less than 40 per cent showed satisfactory evidence of complete healing during the period of observation, and

over 50 per cent are still in the latent stage, have progressed to the advanced stages, or have died. The initial stage of glomerulonephritis is frequently overlooked because of the mildness of the symptoms, and this fact has given rise to the widespread opinion that chronic nephritis develops independently of the acute form. Bierman's studies establish the presence of a latent stage of the disease which may last for years without clinical symptoms and which forms the connecting link between the acute and chronic forms of glomerulonephritis

The fact that latent glomerulonephritis in childhood, as in adult life, often escapes detection unless quantitative examination of properly concentrated urine is made, is emphasized by Snoke 2 The initial stage of nephritis may be overlooked and untreated when gross hematuria or fulminating symptoms are absent If this occurs, latent glomerulonephritis may develop and either heal or pass on into the degenerative or terminal The duration is variable and active chronic nephritis may not appear until adult life Complete recovery is not certain until repeated quantitative examinations of concentrated urine over a period of at least one year have been The intensity of the initial stage, the nature of the infection preceding it, and the age at the onset have no relation to the outcome Hypertension and increased amounts of blood urea have similar significance and tend to parallel each other, in the initial stage they have no relation to prognosis, but later their appearance supplies the first indication that the kidneys are beginning to fail The value for blood urea does not become abnormally high as a rule until 50 per cent of the renal tissue fails to function.

Hypertension, according to Bell,³ may not be present during the entire course of

acute glomerulonephritis and at times is absent entirely. In mild cases the blood pressure may be raised only during the first few days, and usually it returns to normal long before albumin disappears from the urine Persistent hypertension indicates the development of chronic nephritis In acute glomerulonephritis, the flow of blood through the kidneys 15 reduced because of the widespread capillary destruction, and experimental evidence suggests that either this anemia of the kidney or the increased resistance in the renal circulation is in some way responsible for the hypertension some severe cases of acute glomerulonephritis, failure of the heart or vasomotor system to respond to the stimuli from the diseased kidney may account for the absence of hypertension

After administering large amounts of alkalis in one series of scarlet fever cases and thyroid and iodine in another, Peters and Cullium⁴ found no significant decrease in the incidence of *nephritis* following the disease. They conclude that so far no means effective against all strains of streptococcus has been found to prevent this serious complication.

Cockburn⁵ discusses the removal of tonsils and adenoids in 50 of his series of 146 cases of acute nephritis. The immediate results were an increase of blood and casts in the urine. Occasionally a relapse occurred within 24 hours, but this did not appear to prolong the duration of the disease. He concludes that the removal of infected foci plays no important part in the disease.

Impetigo contagiosa is often disregarded as an antecedent to acute nephritis. Goodwin⁶ has studied many nephritic children with this as the only demonstrable preceding infection. The beta hemolytic streptococcus is implicated in acute nephritis more often than any other organism, but one must not

lose sight of the fact that both the pathological and clinical picture of the disease can be produced by other organisms and their by-products, especially the alpha streptococcus and the pneumococcus. It is wise to use serum in severely intoxicated patients suffering from scarlet fever, erysipelas, or pneumonia in the hope of lessening the incidence of acute nephritis

Acute glomerulone phritis is a manifestation of an antibody-antigen reaction according to Kellett, who regards it as a particular example of the general phenomenon of reversed anaphylaxis. He advocates venesection of at least 300 cc of blood when left heart failure develops or when there is cerebral edema. Venesection should be done before lumbar puncture because the latter is apt to cause cerebral hemorrhage.

It is shown by Master, Jaffe, and Dack⁸ that in acute nephritis the progressive changes in the T-waves in the electrocardiogram are definitely indicative of acute myocardial involvement. They believe that there is widespread capillary and arteriolar damage analogous to that in the kidneys. In a few of their cases, perivascular lymphocytic infiltration was found in the heart at autopsy

After studying the etiology in 146 cases of acute nephritis, Cockburn concluded that acute nephritis may follow any childhood disease, not only scarlet fever, and that tonsillitis is a precursor in 30 per cent of the cases

In 78 cases studied by Winkenwerder, McLeod and Baker, upper respiratory infections were found to be the precursor in 67 6 per cent and tonsillitis in 44 per cent Pneumococcic infections, rheumatic fever, endocarditis and latent syphilis were comparatively rare

There were no sex differences in the incidence of acute glomerulone phritis in

Folkers'10 series of 68 cases Respiratory infections were the most common etiological factor. The mortality rate was five to ten per cent and the percentage of serious sequelae was large, the chief one being chronic nephritis.

The prognosis in a hundred cases of acute nephritis was reported on by Richter 11. Ten patients died in the acute stage, five of the *nephritis* and five of the causative infection, 62 of the survivors were cured. 15 became chronic nephritics. Persistent albuminum meant progression into the chronic disease. If albuminum lasts a year or more, the chances of the renal process becoming chronic are six to one.

There is a type of acute kidney disorder which well deserves some attention, i.e. the renal disturbance following blood transfusion Tzanck and Moline¹² divide the clinical phase of this transfusional nephritis into four periods, (a) the period of alarm with subjective symptoms that occur before transfusion has been completed. In such cases renal complications rarely develop (b) anuna or oliguna lasting several days (c) an inconstant hydric crisis duiing which large masses of water are occasionally eliminated by the kidney. ed) the terminal period during which genune uremia sets in sometimes causing death. They advise hypertonic salt solution to be given intravenously. Other suggestions are decapsulation to overcome anuria and high spinal anesthesia based upon the experimental finding that total denervation of the kidneys prevents the disturbances of diuresis by the injection of hemolyzed blood

A case in which urmary suppression followed transfusion with overheated blood is reported by Baker ¹³ He describes the mechanism of post transfusion suppression in the light of older and recent work and concludes that the view

put forward by Baker and Dodds in 1925 furnishes the only adequate explanation of the observed facts According to them, urinary suppression results from an intrarenal obstruction due to excretion of hemoglobin with the urine of high acidity and salt concentration which causes the excreted hemoglobin to be converted into a granular deposit of haematin and to obstruct the renal tubules Hemoglobin ber se is innocuous to the Since precipitates of haematin are more soluble in alkaline than in acid urine, alkalinization should help in dissolving some of the precipitate in the tubules unless there is complete suppression Early recognition and prompt treatment by alkalinization appear to offer the best prospect of recovery

Experiments by DeGowin, Osterhagen and Andersch14 showed that when the unne is alkaline, the intravenous injection of a large amount of dog hemoglobin into dogs seems to be innocuous Four does received a total of 38 transfusions without harm. One developed nitrogen retention while the urine was acid Transfusions of hemoglobin sooner or later produced renal insufficiency when the urme was acid. Only one dog survived seven transfusions when on an acid This syndrome closely simulates that which develops in human beings with renal insufficiency resulting from hemoglobinuria From pathologic studies it appears that the cause of renal insufficiency resulting from hemoglobinuria in dogs is the obstruction of the tubular lumens with masses of pigment derived from hemoglobin These studies substantially confirm the experiments performed on rabbits by Baker and Dodds

Treatment—In the treatment of acute nephritis, one must remember that it is the sequel of an acute bacterial infection and is a disease not only of the kidney but of the entire body. Rubin and

Rapoport¹⁵ list the three major complications of acute hemorrhagic nephritis as renal failure, hypertensive encephalopathy or so-called eclamptic uremia, and cardiac failure.

The treatment of renal failure consists in parenteral fluids given as isotonic glucose and saline intravenously. Even though diuresis does not follow, the resultant dilution of retained metabolites may be beneficial During the period of anuria it is evident that the major disturbance is a retention of waste products which is shown by the blood urea nitrogen The symptoms of hypertensive encephalopathy are promptly relieved and both the systolic and diastolic blood pressure fall rapidly following the intramuscular injection of 0.2 cc of 50 per cent magnesium sulfate per kilogram of body weight and 50 per cent solution of magnesium sulfate given orally and rectally. When cardiac symptoms complicate acute nephritis, the treatment resolves itself into two components (a) Reduction of the peripheral resistance and load, and (b) improvement of heart activity. The first objective is accomplished by (1) Restriction of fluids to maintain the blood volume at a minimal level thus keeping down the peripheral load as long as there are acute cardiac manifestations (2) phlebotomy, especially in those patients with frank cardiac decompensation. Heart action is (1) Rapid digitalizaimproved by tion over a period of 12 hours by giving 45 mg of whole leaf digitalis per kilogram of body weight hypodermically as a fatfree fineture, (2) morphine in adequate narcotic doses, (3) oxygen when necessary to combat the anoxemia of acute cardiac decompensation, (4) small doses of hypertonic glucose (10 to 20 cc of 50 per cent solution) to keep the blood sugar at high levels and replemsh the glycogen stores of the heart muscle

When severe convulsions develop, Goodwin⁶ recommends that *magnesium sulfate* be given intravenously or intramuscularly

The treatment of acute nephritis has also been discussed by Bannick 18 The patient must be kept warm and in bed until the edema is gone, the blood pressure normal, free output of urine established, hematuria diminished, or until the disease has unmistakably become chronic Activity should be increased slowly. The diet in mild cases is not restricted unless the protein is slightly reduced. If there is edema, salt and fluid should be cut down. In severe cases, the kidneys must be put at rest and the diet restricted to small amounts of fruit juices for a few days If oliguria persists, hypertonic fluids should be given intravenously. Diuretics are not indicated. If there is anuria and conservative measures fail, decapsulation should be done When convulsions occur, sedative drugs, venesection, hypertonic dextrose solution, lumbar puncture, and magnesium sulfate must be considered

Although symptoms exhibited by sufferers from kidney disease are of the most diverse character. Platt¹⁷ states that the scope for treatment is small Diuretics are the only drugs which influence directly the manner in which the kidney acts and they are much more valuable in cardiac than in renal disease Acids alkalis and urmany antiseptics influence the composition of the urine but have little effect on the work of the kidney. Other drugs which have been used in nephritis exert their influence on the patient and his symptoms rather than on the kidney itself. In acute nephritis without complications, it is almost an abuse to prescribe any drug unless it be a mild dose of magnesia to prevent constipation Rest, warmth, nursing and the proper diet should meet all the demands

for active treatment. In convalescence or in protracted cases, anemia often develops and large doses of iron and ammonium citrate (90 grains [6 Gm.] a day) are valuable.

In discussing the dietary treatment of acute nephritis, Boyd¹⁸ advises that only fruit juices and carbohydrates be given in the early days of the disease and that later this be expanded to a normal diet except for moderate salt, fluid and protein restriction

The fact that tardiness in the treatment of acute nephritis may result in the onset of the chronic phase is emphasized by Evans ¹⁹ In all cases warmth and rest in bed for at least four to six weeks are necessary

An analysis of the value of decapsulation is given by von Noszkay,20 who studied 12 cases of medical and surgical nephritis He concludes that the effect of decapsulation may be attributed to the following factors (a) Removal of the capsular tension, (b) the sympathectomy action of the capsular resection and the relief of the angiospasm with the resulting increase of diuresis and the cessation of the kidney pains, (c) drainage of the intraparenchymal spaces. When acute alomerulonephritis fails to cure or progress under medical treatment, bilateral decapsulation performed as soon as possible is to be recommended in order to prevent the condition from becoming chronic

CHRONIC NEPHRITIS

Chronic nephritis has been regarded as a disease whose signs and symptoms depend upon the renal pathology and has consequently been treated with the dominant idea of sparing the kidney. Rest, low protein (lacto-vegetarian) diet, and residence in a warm dry climate have been the principal measures. They are still used widely today though the study

and experience of the past 25 years have shown that there are other means of treatment which, although not curative. will yield a longer, more useful life than the earlier regimen of inactivity and pro-These more modern tein starvation methods are discussed by Mosenthal 21 Permanent bed rest is satisfactory for a few months in acute nephritis, but carried on throughout the long course of chronic nephritis will result in disuse atrophy of the muscular and glandular tissues A low protein diet may lessen the excretory demands upon the kidney, but it results in (a) Tissue deterioration, including the kidney itself, (b) the early development of anemia, (c) a susceptibility to infectious diseases, notably tuberculosis. There are six phases of nephritis, the kidney lesion, edema, hypertension, renal insufficiency, anemia and uremia Each one of these, to an extent at least, exists and progresses independently of the others, and the best results are obtained by appraising and treating them individually rather than using an unbending formula in the therapy of all cases and types of chronic nephritis

The protean character of the signs and symptoms of terminal hemorrhagic nephritis are outlined by Page 22 The following points are especially well exemplified in the case he describes (a) An insidious onset means a fatal outcome (b) The terminal stage may last for months (c) Poor nutrition contributes to discomfort and ill health, therefore sufficient protein should be given (d) Salt restriction may relieve edema even though plasma proteins do not rise above the critical If polyuria does not occur, salt restriction may be extreme without producing hypochloremia (e) Even when hemoglobin is not greatly reduced, death may occur in uremia Iron will not help the condition (f) Arterial blood pressure may alternate between a high level and normal (g) Eyeground changes may not be present until weeks or days before death (h) Oliguria may last for as long as 18 days without producing marked symptoms. (i) Increased cells may be found in the pituitary gland.

Vilk and Rabinovich²³ observed 100 cases of chronic nephritis clinically over a period of from six to eight years. A careful analysis of the histories established the fact that in 55 there had been an acute nephritis In one-third of the total no evidence of previous acute nephritis could be found and in these cases the prognosis was less favorable Chronic nephritis is often not diagnosed until it has progressed to a late stage, even to uremia, because the clinical picture may be dominated by cardiovascular symptoms In 13 of the patients in this series the course resembled acute nephritis and rapidly progressed to invalidism and death The recurring edema and high albumin content of the urine, lipoiduria, hypoalbuminemia and marked cholesterolemia was similar to lipoid nephrosis However, the presence of hematuria and a tendency to hypertension showed that the basic process was a glomerulonethritis The duration of life after the onset of acute nephritis in this group was from 3 to 312 years. Chronic nephritis may persist for decades

chronic nephritis was produced in rats by feeding them diets high in protein. These experiments, conducted by Blatherwick and Medlar²⁴ show that functional impairment of the kidney may exist for some time before histological changes indicative of nephritis become apparent. Albumin or casts in the urine were interpreted as indicative of functional impairment of the kidney although they are not necessarily proof of nephritis. When irreparable damage occurred, retention of nonprotein nitrogen, inver-

sion of the albumin-globulin ratio and hypercholesterolemia were observed. The injurious factor may exist as such in the diet or may be produced during metabolism. If harmful substances exist in the diet they may not necessarily be confined to the protein fraction. Nephritis may be introduced by an abnormal excretion of normal end-products, by an excretion of abnormal products, or by the retention of certain substances.

The relationship between the anemia of *chronic nephritis* and gastric acidity was studied by Townsend, Massie and Lyons ²⁵ They found that a normocytic anemia became manifest as renal insufficiency occurred and increased with the degree of nitrogen retention. Along with this there was a decrease in the gastric acidity. Absolute achlorhydria was present when the carbon dioxide content of the whole blood (plasma bicarbonate) fell below 30 volumes per cent. There was no apparent lack of active blood forming tissue.

In a discussion of 18 cases of chronic nephritis in which all degrees of anemia were represented, Nordenson²⁶ states that he found no regenerative changes in the form of reticulosis in the peripheral blood, or marked signs of regeneration in the red blood corpuscles There was pronounced agranulocytosis in all but one case Intravital examination of the sternal bone marrow revealed elective injury of the erythropoiesis, the leukopoiesis was relatively intact. The bone marrow was normal in two of the three cases in which a blood transfusion gave a good reaction The author concludes that the anemia in chronic nephritis depends on a reduced bone marrow function caused by beginning aplasia of the erythropoietic system. In a number of cases a certain parallel appeared between the rest nitrogen and renal function on the one hand and the anemia on the other On the

whole, the longer the duration of the *nephritis*, the more marked was the anemia. To what extent other factors act in the genesis of the beginning aplasia of the erythropoietic system is uncertain

Chronic hypertension was present in all but five of the 66 chronic nephritics studied by Richter and O'Hare 27 Angina pectoris and coronary thrombosis were infrequent, and pericarditis was the most common cardiac disorder heart was enlarged in all cases Gallop rhythm was found in the late stage of one-third of the cases In 43 per cent there were various kinds of murmurs. and congestive heart failure developed in 23 per cent a few months before death Pericarditis was present in 48 per cent of the cases and death occurred at an average of seven days after the pericardial rub was heard The electrocardiogram showed little abnormality before the onset of fericarditis. One or both coronary arteries were thickened. In 14 cases the histological changes in the invocardium were relatively unimportant

According to Harrison and Mason,28 urenna is trequently initiated by congestive heart failure and therapy directed to the heart may be life saying. The manitestations of uremia may be postponed for many months by overcoming the additional impairment of renal function produced by congestion. Severe dehydration due to polyuna, vomiting, or diarrhea is treated by restoring body A low protein and high carbofluids hydrate diet is advisable and parenteral glucose improves liver function. Lumbar puncture and venesection are valuable in treating headache, vomiting and convul-Acidosis may be relieved by sodium bicarbonate

In an interesting article, Misske and Otto²⁹ discuss the pallor of patients with chronic *glomerulonephritis* The paleness may be due to spasms of the blood

vessels of the skin, deposits of pigment, or anemia. They found anemia in 44 per cent of the cases of *chronic glomerulo-nephritis* without marked disturbances in renal function. The average hemoglobin content was 70 per cent while the average number of red blood cells was 3,730,000. The same relations were found between the anemia and the nonprotein nitrogen. Moderate leukocytosis was observed in 54 per cent of all cases.

Recent literature includes reports of high blood urea nitrogen not associated with chronic renal failure. In an article by Wohl and Brust30 a list of non-renal causes is given (a) Vomiting as in gastric cancer, pyloric spasm, toxemia of pregnancy, gastric tetany, acute intestinal obstruction, or acute peritonitis, (b) repeated gastric lavage, (c) diarrhea, (d) cerebral hemorrhage, (e) reflex anuria, (f) diabetes mellitus, (g)extensive burns, (h) pancreatic necrosis, (1) infectious diseases. The differentiation between chronic glomerulonephritis and non-renal azotemia is pointed out If the nonprotein nitrogen and urea nitrogen values are high, the blood chloride values are apt to be diminished and the carbon dioxide combining power of the blood plasma increased. The nonprotein nitrogen content of the blood is the result of three factors, the rate of protein breakdown in the body, the concentration power of the kidneys and the amount of water secreted. With a great protein destruction, as in lobar pneumonia, the nonprotein nitrogen may rise when the kidneys are normal, especially if the water excretion and intake are slight

Renal Function Tests

The large number of articles dealing with new renal function tests and modifications of old ones proves that so far there is no ideal method of measuring

kidney functions After years of practice most physicians rely upon simple It must be borne in mind, methods too, that the reserve power of the kidney cannot be estimated by laboratory tests alone, one must blend information obtained from numerous renal function tests with certain clinical features and appraise the capacity of the kidney only after prolonged observation Our methods of determining renal insufficiency are based upon the following principles (a) The ability of the kidney to concentrate the urine, (b) the ability of the kidney to secrete introduced substances. (c) the effectiveness of the kidney in secreting the waste products of metabolism as estimated by the clearance tests

Freyburg³¹ states that the degree of albuminuria and hypertension is of little importance compared with the functional capacity of the kidney as an accurate index of the severity and prognosis of Bright's disease The most sensitive test of all is the concentration test Low specific gravity indicates renal impairment The phenolsulphonphthalein test is not as sensitive, but when the normal amount of injected dye is excreted, it is safe to say that there is no very great renal damage Extra-renal factors may interfere to such an extent that low excretion is not an actual estimation of the functional capacity this article the author gives a detailed account of these tests

Since the introduction of the blood urea clearance test by Van Slyke and his associates a number of years ago, many studies and certain improvements have been made on this procedure. For a simple and practical description of this test and its clinical value one may refer to Queries and Minor Notes in the Journal of the American Medical Association ³². Here the technic is described and the test is evaluated.

The blood urea, urea clearance, maximum specific gravity, and phenolphthalein tests were done by Don³³ in 64 cases of suspected kidney disease When pronounced renal failure was indicated by a high blood urea, the urea clearance and phenolphthalem tests showed marked reduction of renal function, but this was not true of the maximum specific gravity On two occasions when the patient was edematous and passing very little urine it was normal when the blood urea was over 100 mg per cent The ability to secrete urine was at fault but the concentration was normal In other cases where renal function was apparently not nearly as severely impaired, this test seemed to be very delicate A surprising number of patients showed a lowered phenolphthalem excretion, but this may be due to the fact that many had a high blood pressure There is a lack of parallelism between the tests especially in the lesser grades of renal damage, and none of them appear to be of much greater prognostic value than the blood urea alone However, if any of the tests show marked loss of renal function in the absence of a raised blood urea, the prognosis should be guarded Clinical examination often furnishes the most reliable information The tests do not agree more closely, either because they are not completely reliable or because different renal functions are measured

According to Stieglitz, 4 it is wholly impossible to judge the severity of renal injury by the intensity or duration of such common symptoms as albuminuria, edema, casts, and arterial hypertension alone. Many of these phenomena, especially edema and hypertension, may be due largely to extra-renal factors. Diagnosis should include quantitative as well as qualitative impressions, therefore functional studies are necessary. All

normal living structures have a functional reserve which is most conspicuously manifest clinically in the heart This is true of the kidney also, and there are no pathognomonic symptomatic evidences of functional impairment until this reserve has been depleted to the point of renal decompensation tional failure is clearly conspicuous, but before it occurs there is usually a long period of impaired reserve which may be detected by renal function studies We start life with a renal margin of safety of about 400 per cent, but mevitably the transient infections and insults from the vicissitudes of existence deplete this margin. The depletion is tremendously accelerated by actual renal disease The concentration test is thus far the most sensitive measure of func-The urea clearance is tional reserve more accurate in advanced nephritis, and phenolsulphonphthalem excretion is grossly impaired only when damage is extensive. The glomerular function test with sodium terrocyanide is still experimental

Albuminuria is generally evidence of damage to renal function but is not necessarily in proportion to the degree of it Crainsborough35 states that slight albummuria may occur in acute toric nephritis when there is almost complete loss of excietory power, or gross albuminuna may be present in chronic forms when renal function is otherwise The early stages of nephrisatisfactory tis are often overlooked and patients may be seen for the first time in the terminal stages of the chronic phase of streptococcal tonsillitis it is important that the urine should be examined for three or four weeks from the onset of the attack In any case of albuminuria, the persistent presence of casts in the urine is pathogonomic of renal damage In estimating renal efficiency all the signs and symptoms of the disease should be considered, and in addition tests of urmary specific gravity and volume, blood urea, and urea clearance tests provide valuable information and a guide to treatment and prognosis

Winkler and Parra 36 studied the manner of variation of creatinine. sucrose, and urea clearances in a group of subjects with renal disease and found that the absolute magnitude of all three is usually consistently and uniformly reduced, while their normal order, creatinine greater than sucrose and sucrose greater than urea, is generally maintained In "nephrosis" all the clearances may be normal The behavior of these clearances in the presence of renal disease is consistent with the theory that they all are relative measures of filtration and that the degree of reduction reflects quantitatively the degree of reduction of the glomerular filtration rate

It is the opinion of Lennerre³⁷ that determination of the blood urea is the only method of discovering renal involvement in the eruptive stage of scarlet fever If the kidney involvement is intense, there may be oliguria and uremia In early uremia, renal hypertension is always absent. If albuminuma exists it is late and transitory Edema appears only under exceptional circumstances These characteristics are in contrast to the nephritides of convalescence in which the albumin, hematuria, edema and arterial hypertension are present and are apparently unrelated to the level of the blood urea

Treatment—A resumé of the modern view of nephritis and its treatment is given by Roper³⁸ who says that there are three groups of "medical kidneys," degenerative, inflammatory and vascular or arteriosclerotic. The arteriosclerotic type results from atrophy caused by diminished blood supply in essential hy-

pertension. The treatment is therefore directed at circulation. The main class of the inflammatory group is the diffuse nephritis which occurs as a sequel to some bacterial infection and is a result of toxins attacking every nephron Diminished blood supply because of vascular blockage leads to lowered urinary output and greater permeability. There may be a "silent period" between the acute and chronic phases or the transition may be a gradual merging of the acute into chronicity

In an article on the treatment of advanced nephritis, Plotz, Howard and Marzullo39 state that patients in the later stages of nephritis present a hopeless problem as far as cure is concerned, but their comfort and length of life may be greatly influenced by treatment Frank infection should be treated, avoiding operative measures if possible Arterial hypertension is best treated by bed rest, simple sedatives, magnesium sulfate intravenously, epsom salts by mouth and venesection The diet must be individualized and adequate vitamin intake is necessary. If edema is not a problem, 2000 to 3000 cc of fluid should be given daily. To maintain nitrogen balance, more than the minimal protein requirement is necessary. A mixed diet is best as long as the patient can tolerate it When anorexia and renal failure set in, however, this must be modified and milk should form the basis of the diet Glucose may be given parenterally Rest should be sufficient and exercise restricted and attention given to the skin and bowels For the treatment of hypertensive encephalopathy, venesection is probably the most effective measure Spinal puncture, intravenous or intramuscular magnesium sulfate, chloral hydrate by rectum, hypertonic solutions, and in extreme cases chloroform are also helpful

In chronic nephritis with edema and little or no nitrogen retention, Bannick16 believes that the diet should contain ample protein to insure a positive nitrogen balance and an additional supply for storage About 100 grams daily is adequate for an adult. Salt is rigidly restricted and fluid is given in moderate amounts Diuretics are indicated and both the acid and alkali variety have shown good results If salyrgan is used it should be given cautiously. Digitalis is beneficial if there is evidence of myocardial failure Some physicians have obtained good results with acacia definite foci of infection should be removed and a warm dry climate is pref-If both edema and nitrogen retention are present, a salt-free diet with moderate protein reduction (50 to 60 grams daily) is best, but a positive nitrogen balance should be maintained A liberal fluid intake (some intravenously) is given until azotemia is Suitable diuretics such as controlled potassium nitrate, potassium citrate, or potassium bicarbonate may be used cautiously, and blood transfusion may be beneficial When there is nitrogen retention without edema, proteins are restricted, and a liberal fluid intake (2500 to 3000 cc daily) is allowed by mouth unless nausea or vomiting make other routes advisable Diuretics do no good except for digitalis which is indicated when cardiac decompensation is present Blood transfusion may help temporarily The anemia is very resistant to treat-Since heart failure is always threatening, the cardiac load should be reduced as much as possible

In treating the edema of chronic glomerulonephritis caused by lowering of the blood proteins, Mosenthal²¹ advocates a high protein diet. The formula of Peters—75 grams plus the amount lost in the urine—is a good one. It has

been established that the sodium and not the chloride in salt favors the production of edema. This makes it clear why potassium chloride can be advantageously substituted for sodium chlo-Symptoms of renal insufficiency do not appear until the urea nitrogen in the blood rises to a level of at least 60 mg per 100 cc Consequently the protein in the diet should not be curtailed until that figure is reached, because it is desirable to delay the inevitable anemia and malnutrition as long as possible. The first sign of renal insufficiency is the lowering and fixation of the specific gravity which is compensated for by an increased output of urine to maintain an adequate elimination of Fluids should be enurmary solids comaged in order to maintain this "compensatory polyuna" Liver and from medication will relieve the anemia somewhat, and when regeneration of hemoglobin and red blood cells is unusually resistant, blood transfusion must be considered. When retention uremia results from a lowering of the compensatory polymia, three to four liters of fluid are indicated to give the kidney ample material with which to form urinc When there is vomiting this should be administered as ten per cent glucose in normal salme. Headache, nausea and vomiting are best controlled by chloral given rectally. Thirty to 60 grains (two to four grams) of chloral at a time in a small amount of starch paste is absorbable readily and is usually effective Ten to 20 grams (0.64 to 1.29 (am.) may be given by mouth and repeated as needed. In cases of retention uremia, the diet should be as low as possible in protein and high in fat and carbohydrate It is well to remember that sugar, corn starch and tapioca are made up of carbohydrates without an admixture of protein, and they, together with fruits and fruit juices, constitute the ideal diet for retention uremia

Limitation of protein to between 50 and 80 grams a day is advised by Lyon40 in treating uremia. The nitrogen balance cannot be maintained with less Lumbar puncture and venesection will relieve persistent headache For sleeplessness, restlessness and general irritability bromides, alone or combined with chloral and paraldehyde, are recommended even if relatively large doses are required Ten cc of ten per cent calcium gluconate, given intravenously, is useful in controlling general nervousness. muscle cramps, hiccoughs, and paroxysmal dyspnea If vomiting is persistent, gastric lavage with normal saline or two per cent sodium bicarbonate solution is Dehydration and hypochloremia are best treated with glucose and saline parenterally

Diuresis—A summary of our present knowledge of the subject of diuresis is clearly and completely given by Chiistian 41 He points out that the treatment of renal edema is just the same whether we are dealing with nephrosis, chronic nephritis, or acute nephritis Mercurial duiretics are more effective than those of the xanthine group and as a rule cause no renal irritation. Urea in large doses is an efficient diuretic if it can be tolerated by the patient. Recently salvigan and mercupurin have been made available as suppositories, and in a more recent article Christian42 states that these are very effective in both renal and cardiac edema

In Mosenthal's article²¹ diuretics are discussed in detail. Urea in ten-grain doses three times a day may be effective unless the blood urea is at a high level. Acid producing salts, especially ammonium chloride and ammonium nitrate, as a rule accomplish no more than salyrgan or mercupurin alone. Digi-

talis is worth a trial in most cases The purine derivatives have been widely used, but they have not proved effective except when cardiac failure exists. Theobromine, diuretin (5 to 10 grains [0 32 to 064 Gm], three to four times a day) and theophylline or "theocine" (3 to 5 grains [0 19 to 0 32 Gm], three times a day) are the ones most commonly used They should be given intermittently every third or fourth day The author has found theophylline the most effective Some authorities prefer the mercurials, salyrgan or mercupurin, given in 2 cc doses intravenously or intramuscularly not more frequently than twice a week

There has been much disagreement about the value of acacia in the treatment of hypoproteinemic edema due to chronic nephritis. Boone⁴³ believes that it will eventually prove to be of definite value. It should probably not be used until less unique procedures have been given a fair trial because of the possible adverse effects of introducing a foreign colloid into the blood stream. It is contraindicated in patients with cardiovascular disease because it greatly increases blood volume.

ESSENTIAL HYPERTENSION (The Nephroscleroses)

Most authorities agree that there are two types of essential hypertension, designated as the 'red' and "pale' by the Germans and the "benign" and "malignant" in this country. It is generally believed that both are stages of one arteriosclerotic process differing from one another not in type but in degree A great deal of literature has appeared during the past year on the control of hypertension by operations on the autonomic nervous system.

The paper by Prinzmetal and Wilson⁴⁴ on the nature of arterial hypertension is an outstanding recent contribution. They studied the blood flow in the arms under various conditions, using the arm plethysmograph, and drew the following conclusions (1) The increased vascular resistance in different types of hypertension is not confined to the splanchnic area, but is generalized throughout the nervous system (2) Increased fiber resistance is due to hypertonus and not to organic changes in the vessel wall (3) This hypertonus must be regarded as intrinsic spasms of the blood vessels themselves and is dependent on vasoconstrictive action (4) All types of hypertension, the benign, the malignant, and the renal, are produced by the same type of mechanism (5) In the types of hypertension studied it appears that normal vasoconstrictive action is superimposed on an intrinsic vascular hypertonus leading to acute elevation of blood pressure (6) Surgical procedures aiming at the relief of high blood pressure by sympathectomy do not abolish vascular hypertonus which is responsible for the high blood pressure. They merely remove the superimposed vasoconstriction

In support of the theory that the rise in blood pressure is caused by a widespread vasoconstrictor action. Hines and Brown⁴⁵ describe what is known as the cold pressor action, a test which measures generalized vasomotor tonus using ice water as a stimulus patient is allowed to rest in a quiet room for 20 to 60 minutes. The cuff sphygmomanometer is placed in one arm and the opposite is immersed in ice water to a point just above the wrist Pressure readings are taken at the end of 30 and 60 seconds. The maximum reading obtained while the hand is in ice water is taken as the index of response. The maximal response occurs

within 30 seconds and in normal people the blood pressure returns to the basal level within two minutes. In the hypertensive there is a delay With this test one is able to select patients who have a tendency to develop hypertension.

The mechanism of peripheral resistance and persistent high blood pressure were studied by Pickering 46 He found that under similar conditions the rate of blood flow through the forearm is the same in subjects with essential hypertension, malignant hypertension, and chronic nephritis and hypertension, as in subjects with normal blood pressure After periods of circulatory arrest, the rate of blood flow increases to the same extent In both normal and in all patients hypertensive subjects the rate of blood flow through the cutaneous vessels in the hands declines after inhibiting vasoconstrictor nerve impulses as age advances because of arteriosclerotic changes in the hand vessels. The author concludes that it is not a nervous agent which narrows the vessels in essential hypertension and chronic nephritis

In their experiments on dogs, Prohaska, Haims and Dragstedt⁴⁷ produced a sustained hypertension for periods up to two weeks by the continuous intravenous injection of epinephrine. The amount required, however, was sufficient to cause death from the other systemic effects of the hormone, principally the inhibition of motility of the gastrointestinal tract and derangement in carbohydrate metabolism. For this reason they conclude that it does not seem probable that persistent hypertension in man will be found to be due to hyperadrenalemia

After studying experimental serum nephritis in rabbits, Arnott, Kellar and Matthew⁴⁸ came to the following conclusions. (1) Hypertension is associated with experimental serum nephritis (2) Previous renal denervation does not alter

the intensity of the lesion (3) Previous renal denervation prevents the occurrence of hypertension (4) Renal denervation terminates the hypertension. Their results conform with those obtained with oxylate nephritis in 1936 and strengthen the contention that the hypertension of acute diffuse renal disease depends for its occurrence upon the integrity of the renal nerve supply

Goldblatt⁴⁹ produced persistent hypertension in dogs and monkeys by constricting the main renal arteries. This reduces the blood flow to the functional components of the kidneys (renal ischemia). Hypertension with or without disturbances of renal function, resembling in this respect benign and malignant hypertension, respectively, in man, can be produced by varying the degree of constriction of the main renal arteries.

After studying experimental hypertension Goldblatt, Gross and Hanzal⁵⁰ conclude that the theory behind certain operations for the relief of hypertension in man is that the vasomotor nervous mechanism gathered in the zone of the splanchnic nerves is an important determining factor in the causation of hypertension. They do not dispute the favorable reports of splanchnic operations, but they offer experimental evidence to disprove the theory that the splanchnic nerve centers exert a significant control over the vasomotor mechanisms dogs (and by inference in human beings) excision of the thoracic portion of the splanchnic nerves and the lower four dorsal sympathetic ganglia on both sides will not prevent, cure, or permanently lower experimental hypertension produced by partial clamping of the renal arteries

Splanchnic nerve resections with interruption of the thoracic sympathetic chain were done on nine patients by Page and Heuer ⁵¹ Six were cases of essential

hypertension varying in severity and ranging from 25 to 48 years of age. Of the other three, one, aged 25, suffered from early malignant hypertension, and the other two, aged 18 and 25, from severe malignant hypertension. Marked reduction in arterial pressure followed operation, but within six months it returned to the preoperative level in all patients There was subjective improvement consisting of lessening in frequency and severity of headaches, ease of fatigue. nervousness, tenseness and irritability in six of the patients with essential hypertension, but in three improvement lasted less than a year. The beneficial effect was transient in those patients with malignant hypertension There appeared to be no marked effect on renal efficiency or on the heart, and no consistent change was observed in the pressor response to immersion of the hand in cold water (Hines and Brown test) The therapeutic results in this small but representative group did not appear to the authors to be encouraging

In another article, Page and Heuer⁵² present evidence indicating that, as a part of a more generalized vasoconstriction, vessels of the splanchnic area are narrowed in patients suffering from essential or malignant hypertension attempted to abolish the extrinsic vasomotor control of this area by section of the anterior nerve roots with the hope of reducing the arterial pressure Seventeen patients were subjected to operation The ultimate effect on the course of hypertension cannot be foretold since the patients were observed only from 8 to 37 The following results were months noted (a) Three patients in whom the disease was severe but still benign and without advanced vascular changes re-(b) One of the three sponded well patients with more advanced involvement of long standing with marked sclerotic

and benign vascular changes responded favorably. The headaches were relieved in the second and third cases but the progress of the disease was unchecked (c) Six young patients exhibiting the "hypertensive diencephalic syndrome" appeared to be benefited (d) Three of those suffering from highly malignant hypertension were unaided by the operation and two appeared to be improved

It is pointed out by Wilson⁵³ that the most important factor in the prognosis and treatment of hypertensive disease is not the height of the blood pressure but the degree of arteriolar and arterial sclerosis, especially in the coronaries and the cerebral and renal areas with dysfunction resulting from oxygen and nutriment deprivation. If the coronary arteries are competent, a high diastolic pressure will aid in maintaining adequate nutrition. A small pulse pressure may indicate an impaired myocardium. In view of these facts, treatment directed chiefly at reducing the blood pressure does not rest upon a reasonable basis and may be harmful.

After studying many cases of hypertension along with control cases, Moritz and Oldt54 found that arteriolar sclerosis and hypertension were invariably associated only in the kidneys Renal arteriolar sclerosis was present in 109 of the 200 cases studied, and 97 of these proved to be cases of hypertension No comparable correlation could be found in any other organ or tissue. A study of the histological characteristics of arteriolar disease in hypertensive and nonhypertensive individuals, supported the conclusion that renal arteriolar sclerosis is the most common cause of chronic The effect of the renal hypertension arteriolar sclerosis in human hypertension appears to be the functional analogue of the renal arterial clamp in experimental hypertension. In both in-

stances hypertension appears to be produced by reduction in renal blood flow. They conclude that the only significant site of arteriolar sclerosis so far as the causation of hypertension is concerned is the kidney. The material for this investigation did not include cases in which the hypertension could be attributed to chronic nephritis, congenital polycystic renal disease, urinary obstruction, obesity, hyperthyroidism, aortic insufficiency, aortic coarction, pituitary or adrenal tumors, or arteriovenous aneurysm

Renal Ischemia in Hypertension-Blalock and Levy⁵⁵ performed a number of different types of experiments in an effort to determine the mechanism by which renal ischemia results in hypertension They found that (1) When hypertension is produced by partial occlusion of the renal artery of an explanted kidney, the removal of the kidney under local anesthesia usually results in a slow decline in the blood pressure with a icturn to normal in six to ten hours The rise in pressure is usually slower than the decline (2) The rise in pressure which may be associated with occlusion of a ureter is abolished by the removal of the kidney, the pressure returning to normal in approximately six hours (3) When the blood pressure returns to normal following partial constriction of the artery to one kidney removal of the opposite normal kidney usually results in a rise in the pressure (4) Partial construction of the blood supply to the single remaining kidney which has been completely denervated by transplantation to the neck results in a rise in the blood pressure. Release of the constriction or removal of the kidney under local anesthesia results in a return to normal pressure (5) Bilateral adrenalectomy abolishes experimental renal hypertension Subdiaphragmatic (6) section of the splanchnic nerves, removal

of the celiac and upper lumbar ganglia and partial bilateral adrenalectomy do not abolish or prevent hypertension due to renal ischemia

Renal Status and Blood Pressure -Data regarding the renal status and blood pressure in 48 patients with hypertensive vascular disease treated with hilateral splanchnicectomy are presented by Freyburg and Peet 56 Hypertension was greatly relieved in some cases, benefited to a lesser degree in others, and uninfluenced in the rest In general, the renal changes were associated with changes in blood pressure In those patients who maintained a significant lowering of blood pressure, urmary abnormalities decreased or disappeared and the renal function improved When the hypertensive condition was not improved, renal function remained unchanged, or gradually became worse as would be expected in unoperated cases These observations show that in cases of primary hypertension, satisfactory renal function is not dependent on the high blood pressure, that hypertension is not compensatory to renal damage, that marked impairment of renal function may accompany hypertensive vascular disease, and that striking improvement of renal function follows relief of hypertension brought about by splanchnicectomy

By experiments on dogs, Glenn, Child and Heuer⁵⁷ have shown that hypertension may be produced by the constriction of the arteries of a transplanted kidney, nephrectomy having been done on the opposite side. It appears that it is more difficult to produce a sustained hypertension after unilateral nephrectomy and renal transplantation than after constricting both renal arteries.

Celiectomy and denervation of the aortic plexus may well be recommended to patients with such symptoms as severe headache, dizziness, weakness and nerv-

ousness, according to Crile ⁵⁸ An excellent prognosis in this respect can be assured them. The operation is more strongly indicated in cases of malignant hypertension as evidenced by edema of the optic discs. This operation was performed on 149 patients, but none of them have been followed more than one year.

Allen and Adson⁵⁹ believe that it is apparent that essential hypertension can be treated surgically without undue Patients are not disabled and in many cases the blood pressure is significantly reduced The operation must not be considered a cure for essential hypertension, for it often does not reduce the blood pressure when the disease is advanced or results from irreversible renal changes The procedure is too recent to draw conclusions as to the permanency of the symptomatic improvements. However, the results have been sufficiently encouraging to justify further trial of surgery in the treatment of essential hypertension

Results of ventral rhizotomy or extensive subdiaphragmatic resection of the splanchnic nerves with removal of the upper two sympathetic lumbar ganglions and a portion of the suprarenal gland vary according to Craig and Adson 60 Patients with short histories and mild symptoms obtain a greater drop in blood pressure Clinical improvement is probably more manifest than actual drop in blood pressure. Ocular symptoms are improved. Moderate improvement in the kidneys, heart, and brain can be expected if the damage has not been too great, although it appears that the autonomic nervous system and particularly the sympathetic system plays an important role in the homeostasis of the human body, it is possible for human beings as well as experimental animals to live without its influence in limited areas at least

It is the view of Pickering⁶¹ that 50 per cent of the patients suffering from cerebral vascular lesions have retinal arteriosclerosis and that a high proportion of them eventually develop apoplexy Patients with albuminuric retinitis always die within a year or two of the lesion's appearance except in pregnancy hypertension when the whole condition may clear up. On the other hand patients with arteriosclerotic retinitis may live as long as 15 years Albuminuric retinitis accompanies malignant hypertension, the terminal stages of chronic nephritis and eclampsia It is rare in acute nephritis, and unknown in benign hypertension Arteriosclerotic retinitis is common in benign hypertension, but it occurs rarely in chronic nephritis and never in malignant hypertension, acute nephritis or pregnancy In general, albuminuric hypertension retinitis occurs in patients with a greatly raised diastolic pressure or with severe hypertension of relatively recent onset Arteriosclerotic retinitis occurs in patients who have had a moderately raised blood pressure for a long time Examination of the retina is chiefly important in distinguishing between benign and malignant hypertension — a differentiation which frequently can be made in no other way

Lesions of the retinal arterioles and resultant lesions of the retina in cases of essential or nephritic hypertension are described by Wagener⁶² as indicative of a diffuse disease of the arterioles throughout the body. Sclerosis of the retinal arterioles is a sign of chronicity rather than activity and its severity is a fairly accurate criterion for the arterioles throughout the body. Angiospastic changes indicate active and progressive hypertensive disease. Edema of the optic dises with angiospastic retinitis is usually a fatal prognostic sign. Careful ophthalmoscopic

study is an aid in the classification of hypertensive states and nephritis

Because most of the methods advocated for the treatment of permanent essential hypertension are difficult of execution, Hermann and Sabadini⁶³ have limited themselves to resection of the splanchnic and sympathetic nerves. The pathogenesis of permanent essential hypertension is not sufficiently understood to justify conclusions as to its surgical treatment

Hypertensive heart disease has been studied by Murphy, Woods and Grill⁶⁴ who state that it is the result of the combined action of hypertension and arteriosclerosis of the coronary arteries The heart which has been over-strained by persistent hypertension hypertrophies, becomes inpoverished by lack of proper nutrition due to coronary sclerosis and fails as a result of a combination of these two forces. The theory that hypertension and arterioselerosis result from modern living seems to be without grounds. The two prominent etiological factors are hereditary disposition and advancing age Every hypertensive is a subject for heart tailure within five to fifteen years of the onset. In these years of transition treatment is most effective. Infections, overeating, overweight, overexertion and overwork are to be avoided and digitalis and After the heart has sedatives given tailed the treatment consists of digitalis, diuretics, oxygen and the other methods commonly used in cases of heart failure

In writing on the subject of the hereditary factor in essential hypertension, Hines⁶⁵ states that a positive family history of hypertensive cardiovascular disease is five times more frequent among individuals who have hypertension or who are hyperreactors to a standard stimulus test than it is among individuals who react normally to the test. The excessive or hypertensive type of reaction

occurred predominantly among members of families in which there was a hypertensive diathesis. These findings are considered to be strong evidence that the hereditary factor plays an important rôle in the development of essential hypertension. The inherited quality may be a vasomotor system which reacts excessively to certain external and internal stimuli and eventually results in the development of essential hypertension in many cases.

The efficacy of medical treatment of essential hypertension is brought out by Palmer 66 He studied 169 cases and classified them according to age and the degree of hypertension In the mild form of the disease 90 per cent of all ages either have no symptoms or are easily relieved. In the moderate form there is a 50 per cent chance of a fall in blood pressure in all age groups and 75 per cent can be much relieved a patient under 46 years of age radical therapeutic measures must be considered since in this age period the malignant form occurs most commonly, especially Medical treatment is amone temales of no value and any surgical help giving symptomatic relief is most welcome. In the group over 46 years of age, a fall in blood pressure is possible in one-third of the cases and symptomatic relief in 46 per cent. The vascular changes are irreversible and surgery will do no good

In an article on the treatment of essential hypertension, Adson and Allen⁶⁷ advocate that treatment should begin with a period of several days of **rest in bed**. It is wise to speak of reducing or controlling blood pressure rather than of curing hypertension, for once the patient believes cure is possible, he is rarely satisfied with less. If the patient is obese his weight should be reduced, and if he is not, a general diet may be given. Salt and protein restriction are

not generally considered advisable The nitrites, acetylcholine and acetylbetamethylcholine have in common a vasodilating action which is too short to be valuable Bismuth subnitrate and ovarian hormones have little or no effect on blood pressure There is some evidence that potassium thiocyanate may be beneficial but the dosage must be carefully regulated Rest is the most important prescription, but apprehension and semi-invalidism can be caused by a regimen which is too strict. Ordinarily patients should rest or sleep nine to ten hours each night They should lie down in a quiet darkened room for an hour at noon and when possible should rest in a quiet peaceful environment during the weekends The physician should weigh the pleasure which the nonessentials in the patient's life give against the benefit to be derived from their elimination Under controlled conditions it can be demonstrated that administration of large amounts of sedatives particularly the barbiturates will cause the blood pressure to return to normal in many cases The amount of sedative to be given should be great enough to abolish nervousness and restlessness and small enough to avoid drowsiness and excessively slow mental reactions. Many patients do not respond adequately to medical treatment

NEPHROSIS

The subject of lipoid nephrosis has received much consideration in the past few years, but there is still much disagreement as to whether the disease exists as an entity apart from glomerulonephritis. According to Epstein⁶⁸ the term nephrosis as now generally applied represents a compromise between pathologists and clinicians. From the pathological standpoint it includes all forms

of renal disease with tubular degeneration while according to the clinical concept it refers to a group of diseases with edema, oliguria and albuminuria possessing characteristic biochemical changes in the blood. The pathological prototype of nephrosis is the degenerative process of the kidney tubules which results from certain metallic poisons and bacterial toxins The clinical course is specific and differs widely from that manifested by the group of cases generally designated as chronic nephrosis Chronic nephrosis in its purest form is a disease which begins insidiously, is of unknown origin and runs a long course characterized by albuminuria, oliguria and edema, without circulatory changes or impairment of renal function but with certain distinctive changes in the blood. The question is raised whether or not genuine chronic nephrosis is a renal or a metabolic disorder The etiology of true nephrosis is not known and while the albuminuria is of necessity a renal phenomenon, it is not always a proof of the Some eviexistence of renal disease dence suggests a metabolic derangement as the pathogenic factor. In the opinion of most pathologists the kidneys in genuine nephrosis show tubular degeneration and lipoid infiltration but no evidence of inflammation. However, other pathologists claim that it is a degenerative type of nephritis in which the inflammatory processes subside and degenerative tubular lesions persist treatment resolves itself into three definite propositions (1) to replace the protein loss of the blood plasma by means of an adequate protein diet or in extreme cases by blood transfusions, (2) to compel the tissues to utilize the protein and incidentally to reduce the lipoidemia by a liberal protein and tat poor diet and at times by the administration of thyroid extract, (3) to estab-

lish normal metabolism by protein feeding and if this fails, by the administration of thyroid extract. The main value of thyroid is the stimulation of protein utilization, but it does not aim to replace protein feeding which is fundamental in the treatment. The amount of thyroid necessary to combat the metabolic depression in nephrosis is frequently many times that required in myxedema Unlike chronic glomerulonephritis and amyloidosis which are progressive and ultimately fatal, primary or genuine lipoid nephrosis is a curable disease and upon this basis it is not a renal disease. It deserves consideration as a clinical entity not only by virtue of its special clinical characteristics but because of the end result obtained One cannot reconcile these results with any concept or classification of genuine nephrosis as a chronic glomerulonephritis To illustrate this, ten cured cases of chronic nephrosis are presented

Among recent articles on lipemic nethrosis, one by Fahr⁶⁹ deserves consideration. He believes that all the symptoms can be easily explained on the wellfounded assumption that the ultrafilter of the glomerulus, which has been shown in most cases to be altered morphologically by the newer staining methods, has become hyperpermeable. Therefore, the serum albumin from the blood filters off into the urine day by day reduces the content of the serum albumin in the blood until the colloid osmotic pressure is lowered to about one half When it is reduced to this critical level much of the ingested water and salt are filtered off into the skin and other tissues causing edema. The lowered basal metabolic rate in patients with chronic nephrosis is due to the fact that the food intake is usually small and the heightweight formula, due to the water in the tissues, lowers the basal rate The circu-

lating thyroid hormone may be removed from the blood stream along with the serum proteins. It is Fahr's opinion that chronic genuine or *hpemic nephrosis* is a disease of the glomerulus of the kidney and there is no marked change in tubular function. Two cases, fully studied, lead to the conclusion that the real and essential pathologic process in chronic lipemic or genuine *nephrosis* is the thickening and increased permeability of the basement membrane and that *hpemic nephrosis* is only part of the picture of glomerulonephritis.

The after-history of six cases of lipoid nephrosis was studied by Major. 70 Two patients died showing at autopsy evidences of chronic glomerular changes Three have apparently recovered and one still shows a trace of albumin Blood transfusions and intravenous glucose gave temporary relief Thyroid extract and parathormone did no good There seemed to be no bad effects from novasurol or salyrgan Gum acacıa was given in one case and the next day the patient developed acute nephritis with exitus very high protein diet (600 to 800 grams a day) seemed to have remarkable results

Landis and Elsom⁷¹ discussed five cases presenting the clinical symptoms and signs of the nephrotic syndrome. In conjunction with salt restriction the administration of acacia was followed by conspicuous diuresis. Although benefit 15 temporary, acacia is useful as a diuretic measure when given cautiously to patients with normal concentration power and pronounced hypoproteinemia In addition to giving symptomatic relief, otherwise difficult to obtain, it may help avoid the dangerous infections to which patients with persisting nephrotic edema are particularly subject Unquestionably other diuretic procedures are preferred if they are efficacious and acacia, owing to certain undesirable features, should be reserved for otherwise intractable or dangerous grades of nephrotic edema

The logical therapy in nephrosis is directed toward restoring serum protein according to Boyd ¹⁸ Therefore the diet should contain protein in amounts adequate to compensate for that being lost in the urine, to replenish the tissue deficit and to permit normal synthesis Normally the minimal daily requirement is one gram per pound of body weight. There is disagreement as to the desirability of salt and fluid restriction. It is the author's opinion that unlimited water intake is probably innocuous and desirable, but that the evidence points to the desirability of limiting salt intake

If the usual diuretic measures fail to relieve nephrotic edema, Lepore⁷² advocates the use of *acacia*. The dose for the average adult is 500 cc of six per cent acacia repeated at daily intervals for three or four days. A high protein, saltpoor diet and urea or saline diuretics should be given an adequate trial before resorting to acacia.

Thyroid extract up to 15 grains (0.97 Gm.) or more daily is recommended by Platt ¹⁷. He also states that the most efficient diuretic therapy consists of the combination of ammonium chloride or nitrate in doses of four to six grams a day and an injection of an organic mercurial diuretic or the salvigan type twice a week. Before these more drastic diuretics are used a course of urea given in doses as large as ten grams, three times a day, might be tried

Goudsmit⁷³ reports a case of nephrotic edema in which response was not obtained to the usual dimetics in spite of a rigid antihy dropigenous regimen. After the intravenous administration of about two grams of gum acacia per kilogram of body weight, liberal dimesis with the disappearance of edema ensued promptly.

In an extensive article on the diet in the management of nephrosis Barborka⁷⁴ points out the following important factors: (1) high protein content; (2) low fluid intake; (3) low salt intake, (4) low fat intake, (5) high carbohydrate content. The fluid intake must be limited to an amount that will approximately balance the output of the kidney without the influence of diuretics. He gives diet tables which are very satisfactory guides in treatment

RENAL RICKETS

Renal rickets has been fully discussed and an excellent review of the literature given in a recent article by Goldberg and Candido 75 The majority of cases show renal insufficiency—some due to congenital deformities of the urinary tract and others to early and persistent urinary tract infection. The kidney pathology bears a definite relation to the disturbed calcium and phosphorus metabolism resulting in skeletal and sexual dwarfism They present a case of chronic urinary infection in a boy six years of age apparently dating back to early in-This produced a bilateral pyohydronephrosis with hydro-ureters and secondary renal insufficiency which disturbed mineral metabolism causing decalcification of the skeleton in spite of adequate amounts of vitamin D. Genu valgum, or knock knee, was the outstanding rachitic manifestation. Chemical studies of the blood revealed an increased nitrogen concentration with impaired renal function. Although a disturbed relation between calcium and phosphorus could not be demonstrated, x-ray studies of the bones revealed the characteristics of juvenile rickets consisting of diminished lime salts, trabeculation, osteoporosis and patchy ossification The prognosis in renal rickets is very

poor Most cases die from some intercurrent infection or from uremia and seldom reach adult life. The treatment is chiefly protective and symptomatic Attempts should be made to remedy any abnormality or infection of urinary tract

In an extensive article on renal rickets by Price and Davie⁷⁶ a case is discussed and the literature dealing with this condition is reviewed. The earliest symptoms usually occur at about the age of seven and consist of polyuria and polydypsia associated with retardation of growth There may be attacks of renal pain in some cases which are associated with secondary pyelonephritis or calculus Rapid development of genu valgum and thickening of the bony extremities with distortion and deformity may be pro-The kidneys are incapable of excreting concentrated urine and there is always some albuminuria and cast for-The blood chemistry shows azotemia, lipemia and hyperphosphatemia usually associated with a low calcium figure. The one constant etiological factor is pronounced renal damage and defici-There are two theories of the (1) the renal origin of the disease theory, according to which skeletal changes, dwarfism and infantilism are the result of chronic renal disease in childhood, and (2) the endocrine theory which presumes a primary overactivity of the parathyroid glands with or without pituitary dystunction. The authors suggest that the concept of renal rickets as a syndrome representing the common ground of overlap of hyperparathyroidism on the one hand and of chronic renal damage on the other is the most satisfactory in the present state of knowledge

TUBERCULOUS NEPHRITIS

A summary of the treatment of tuberculous nephritis given by Ramond⁷⁷ includes the following suggestions (1) complete rest in bed with the windows open, the kidney region protected by a wide flannel band (2) Lacto-vegetable, salt-free diet at first and as soon as possible a nourishing mixed diet compatible with the state of the kidneys (3) Daily administration of 15 grains (2 Gm) of calcium chloride. (4) Abstention from all antituberculous chemical medication which acts on the kidneys (creosote, gold salts) These are contraindicated on account of their effect on the nephritis

In discussing the surgical treatment of renal tuberculosis, Hale⁷⁸ states that extreme caution must be exercised in Every available this type of case method to establish clinically the absence of bilateral renal involvement must He does not agree with the be used idea that tuberculous lesions in the kidney heal with medical care when tubercle bacıllı and pus have been demonstrated and the pyelogram is diagnostic His cases were treated medically before nephrectomy, but such treatment was instituted only in an attempt to make the patient a safer operative risk carefully supervised period of postoperative rest measured by a clinician versed in the care of tuberculosis is a prime requisite to complete airest or prevention of the spread to other organs. The contraindications for surgery in renal tuberculosis are (1) bilateral involvement, (2) marked involvement of other organs

Gile⁷⁹ reports the follow-up results of 96 patients in which nephrectomy was done for a tuberculous kidney. Apparently the existence of *tuberculosis* elsewhere in the body, the length of time it takes the operative wound to heal, the history of hematuria or the duration of the symptoms before operation have little prognostic value as to the outcome *Renal*

tuberculosis must be considered as a part of a generalized tuberculosis or tendency toward it Where economic conditions permit, every effort should be made to guard against further manifestations of the disease by an antituberculous mode of living.

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DISEASES OF METABOLISM

By Joseph T Beardwood, Jr, AB, MD

DIABETES

Incidence—A recent review of the literature emphasizes again the increasing importance of diabetes not only as a disease but also as a public health problem P B Matz¹ reviews 1663 living diabetic war veterans. The average age of this group was 44. The average age at onset of the disease was 33.7 years which is considerably below the average age of 50 to 54 which is that of the general population. In this group he only found 0.8 per cent of renal diabetics. The Metropolitan Life Insurance Company (Bul 17) shows the increasing incidence of diabetes among me causes of death and emphasizes again that the relative positions of tuberculosis and diabetes will be reversed in the next ten years as a cause of death if the present frend continues This is already true in Nebraska, and in four other states the death rate of the two is almost parallel for 1933 and 1934 It was higher in 12 out of 93 cities with populations of over 100,000—the most outstanding city being Syracuse, N Y, where the death rate among diabetics was

60 9 per cent higher than among patients with tuberculosis Another interesting study is that of Lillian A Chase² who reports the trend of diabetes in Saskatchewan from 1905 to 1934 The population shows many racial origins—the temperature variations are from 56° F below zero to 104° F above zero $(-488^{\circ} \text{ to } +40^{\circ} \text{ C})$ The death rate has risen in the last three years from 37 to 83 which, while still lower than the United States rate of 20, shows twice as rapid an increase. This is of particular interest because the average citizen of Saskatchewan is a farmer and iclatively young and usually relatively poor, and also in the examination of 1500 Indians no case of diabetes was found

It is important to remember that while the death rate from diabetes is said to be increasing a closer analysis of some of these cases will show that these patients die with diabetes and not because of it, and it oftimes leads to erroneous conclusions if the certificate of death implies that because the patient has had diabetes, that has been a factor in his death-when

really his actual cause of death has no connection with his metabolic condition.

Diagnosis—The diagnosis of diabetes presents no difficulty if one has the cardinal findings of glycosuria and hyperglycemia; however, there are many cases of glycosuria who do not present the classical symptoms of diabetes and one is puzzled as to whether or not these are cases of diabetes or of benign or renal glycosuria For many years following the work of Allen in 1913 and Haman and Hirschman in 1919, as well as that of many other investigators, the threehour sugar tolerance test has become fairly well established This test requires three hours to perform and necessitates taking five blood sugars, namely, fasting, 30 minutes after the administration of 100 grams of glucose, then 60, 120 and 180 minutes later As this is ofttimes inconvenient and time-consuming Exton and Rose introduced a shorter test based on the same principles. In doing this test a fasting sugar is taken, 50 grams of glucose in a 15 per cent solution is administered, 30 minutes later another blood sugar is taken and 50 more grams of glucose administered, and a final test taken 30 minutes later. If the third sugar is more than ten points higher than the second it indicates a diabetic condition. This test was carefully compared with the three-hour test by Kelly. Beardwood and Fowler and found to be equally accurate and satisfactory as well as less time consuming

It has been the editor's policy for some years in doubtful cases to have the patient take a breakfast containing at least 75 grams of carbohydrate and to do a single blood sugar two hours later. It the case is one of frank diabetes, this reading will be better than 130. It will not pick up, however, borderland cases, and a regular tolerance test may have to follow.

The work of W. G. Exton3 in analyzing the reducing substances in the urine of 1000 men and women is very interesting. He found that in those cases in which the reducing substance was one per cent or more the substance causing it was dextrose in 97 per cent. In 800 cases in which the value was less than one per cent, only 60 per cent were due to dextrose His analysis of the 400 cases in which the reduction was not from dextrose showed among other things that 71 per cent was due to glycuronic acid-21 per cent due to pentose-18 per cent fructose-06 per cent galactose-and of particular interest in view of recent therapeutic endeavors that 16 per cent was due to vitamin C. Because of the recent extensive use of vitamin C it is probable that this may be even more of a factor in the future

In spite of this work of Exton's, it cannot be too strongly emphasized that any patient who at any time shows reducing substances in the urine should be suspected of being a case of diabetes mellitus until proven otherwise, and that such proof should consist in first doing a fasting blood sugar. If this is above 125 mg per 100 cc there is no use, and indeed some danger in doing a sugar tolerance test. If, however, this is normal, one of the sugar tolerance tests suggested above should be done, and if this is normal it should be repeated again in three to four months. By this procedure many early cases of diabetes will be picked up, and, needless to say, handled much more simply than it the disease is further advanced

Surgery in the Diabetic

The risk of surgery to the diabetic has been greatly diminished during the last ten years—due to the use of insulin, better diet control, and the general appre-

ciation of the mechanism producing certain surgical lesions peculiar to the diabetic One of the most common surgical conditions in patients with diabetes is gangrene, and recent attempts at prevention of its development and of the medical treatment of early cases have been Some of the most outmost helpful standing work in this field has been done by L G Herrmann, and a very complete review of the subject was summed up in his recent book4 in which he summarizes the work of the preceding 100 years, and gives his experience with the positive and negative pressure boot Last year McKitrick listed his recent surgical experience in 1002 operations, and points out that while the mortality shows a downward trend there may be a deviation of from 6 to 22 per cent in succeeding years without any change in the type of cases or of the routine method of handling

The proper evaluation of the abdommal symptoms in the diabetic often presents a very puzzling problem. F. A. Bothe and J. T. Beardwood, Jr. 5 report observations on 1260 consecutive admissions which indicate certain basic differences in the degree of severity of abdominal symptoms due to diabetic acidosis and the symptoms of acute abdominal conditions occurring in the It is of great importance for the surgeon to recognize and appreciate the symptoms of diabetic acidosis. The most common symptoms of diabetic acidosis are nausea, vomiting, and abdominal pain and tenderness, and these are usually associated with leukocytosis and fever. These findings are apt to be present before the comatose symptoms develop, and not infrequently result in the patient seeking surgical aid These patients appear acutely ill, and apparently have a very severe and fulminating type of intra-abdominal lesion

Indeed, they appear even more acutely ill than do the cases having actual abdominal lesions These writers emphasize that no abdominal surgery should be undertaken in a diabetic with abdominal symptoms without making proper laboratory examinations to rule out the presence of acidosis, and they point out that the height of the blood sugar is no indication of the presence or absence of acidosis. In this series there were 18 cases who had acute abdominal conditions and were operated upon, and although many of these patients had free pus or localized abscesses in the abdominal cavity, fever and leukocytosis were not marked, and none were in acidosis

The abdominal symptoms in these patients were not nearly so severe as those seen under similar conditions in the nondiabetics, and this decreased severity of the abdominal symptoms in the diabetic has become more apparent with the greater number of cases seen While the number of cases reported in this series is not large, the authors feel justified in suggesting that an acute abdominal condition occurring in a diabetic will give symptoms much milder than a lesion would be expected to give in a nondiabetic, and definitely less acute than those seen in acidosis alone, which would make it appear that the surgeon might be justified in operating on a diabetic with less indications than he would on the nondiabetic, and at the same time anticipate finding more extensive pathology

Care of the Feet in Diabetes

While gangrene is the greatest surgical problem of the diabetic, it is a condition which can in the vast majority of cases be prevented by control of the disease—proper chiropody—and education of the patient. This is strikingly shown by H. Brandaleone, S. Standard, and E. P. Ralli, who compared a group of

diabetic patients whose foot ailments were attended to with a group that had no such care He and his colleagues find that, in the group in which neither the diabetes nor the feet had been treated. 416 per cent required amputation and 38.4 per cent of these patients died. In their clinic group prior to prophylactic foot care, 32 4 per cent required amoutation and 88 per cent died Previous control of the diabetes improves the prognosis in a patient with infection of the feet, but, if prophylactic care of the feet is carried out systematically at the same time, the prognosis is improved greatly Care of the diabetes alone improved the prognosis 77 per cent When prophylactic foot care was added to this, prognosis improved 90.5 per cent. The major portion of infections occurred between the ages of 50 and 70 There was a definite rise in infections after 40 years of age The large and small toes were involved almost equally. The care of diabetic patients should include prophylactic foot treatment as a routine part of the treatment. This involves the recognition of vascular madequacies of the extremities and their dangers to the patient and should always be under the supervision of a physician. The most frequent cause of infection of the feet in these patients is improper shoes. This superimposed on arteriosclerosis, which undoubtedly exists in patients of the age group most frequently involved, is too much for the resistance of a patient with diabetes mellitus

Lach diabetic clinic has certain routines which they follow in the care of the feet. W. R. Jordan⁷ gives a routine which he follows in Richmond. He points out that the application of simple rules of hygiene and the prompt and correct surgical treatment of each lesion when it first appears will postpone or prevent disastrous situations. Regular

visits by the patient for examination, treatment and instruction by the physician tend to prevent trouble. Cleanliness, correction of preformed defects and immediate attention to all lesions will prevent or at least postpone severe infection and gangrene A corn and callus by pressure causes local irritation and ischemia so that necrosis and infection may Similarly a bunion or hammer toe increases the danger of infection Epidermophytosis with coarse nails and soft corns leads to many amputations addition to the daily bath, thorough drying and clean socks, one must often employ other methods to combat this stub-The liberal use on the born disease feet and in the shoes of talcum containing one per cent of salicylic and benzoic acid is sometimes adequate. When a stronger remedy must be used, the daily application of a petrolatum ointment containing six per cent each of salicylic acid and sulfur should be continued until there is apparent cure of the disease. It is important to apply this not only on all obvious lesions and between and under the toes but also around the entire nail bed. After the disappearance of the lesions, applications should be continued indefinitely twice a week to prevent recurrence. It is a good rule for all diabetic patients to refram from crossing the legs after they attain the age of 40 years. Constriction of any kind should be avoided Exercises are of help in maintaining or restoring circulation. In instances of deficient circulation or damaged nerves. all irritants, hot water bags, electric pads and jodine or other chemical irij-Prevention and tants are interdicted care of foot ailments in diabetic patients are dependent on control of the diabetes The blood and urme sugar must be controlled, and also the diet must be suffi ciently liberal to maintain good health

Protamine Insulin

Undoubtedly the most important advance in the treatment of diabetes in the last ten years was the discovery of protamine insulin by Hagedorn and his collaborators which was first announced in 1936 They found that by using a monoprotamine to precipitate insulin they could produce an insulmate which, when adjusted to the pH of the tissue fluids, was slowly soluble and produced a prolonged effect on lowering blood sugar The protamines are protein-like substances found in nuclei of certain families of fish. The most satisfactory of these was found to be the "salmine" group and are monoprotamines, and the one which Hagedorn used was derived from the sperm of the rambow trout. It was found that the th of the insulmate must be adjusted as stated above to 73 instead of the pH of regular insulin, which is about 35 The commercial manufacturers of insulm, co-operating with the insulm committee of Toronto, undertook to manufacture this product and distribute it to a large number of clinicians for clinical trial A very complete résumé of the literature is contained in an article by R. M. Wilder and D. L. Wilbur S.

The original protamine insulin was supplied in two vials—one containing 4 cc of U 50 Insulin and the other 1 cc of protamine. These two yials had to be mixed shortly before use and were stable for only a comparatively short time. It was later found following the work of Gray and others that the addition of small amounts of zinc-02 mg per 100 units of insulin—imparts stability to the precipitate and that such insulin can be prepared in the commercial laboratories and remain stable for some This has now been released for general use under the name of protamine zinc insulin. At the present time it is dispensed in two strengths, U 40 and U 80, and is a flocculent, cloudy mixture which should be slightly agitated before use. It is important to remember that protamine zinc insulin differs in several important ways from regular insulin, and this will be discussed a little later.

The amount of zinc present in this compound is not great enough to be of any real danger to the patient and the fear of long-continued use of it seems entirely unjustified Regular insulin has always contained a certain amount of zinc, and indeed the recent insulins. which have been purified to a marked degree, such purifications consisting among other things in decreasing the zinc content, have had a much shorter action than did the insulins of a few years ago I M Rabinowitch, J S Foster, A F Fowler, and A C Corcoran9 have shown very clearly that much larger amounts of zinc may be taken into the body without producing deleterious effects of any kind

Duration of Action—Protamine zinc in man, if given in adequate doses to control the hyperglycemia, has a duration of action usually from 18 to 36 hours. It varies from regular insulin in that it is slower in beginning its action, and once it has started it is very much prolonged which results in reactions occurring much later and because of the gradual fall of blood sugar much more insidiously than with regular insulin

It is important to remember also that protamine insulin will take from five to ten days to reach its full efficiency, during which time the dose determined upon may seem inadequate, but when its full effect is reached, the total unitage may usually be materially reduced

Hypoglycemic Reactions Following Administration of Protamine Insulin—The subject of reactions is un-

duly minimized in many reports with the use of this new type of insulin as is pointed out by Wilder (ibid) He states that reactions occur less frequently than with the other form of insulin, and the experienced patient is usually given a longer period of warning before the reaction occurs, although this may not always be the case. He states that one death has already occurred following the use of insulin and fears that others will follow unless the patient and physician are impressed with the importance of heeding the early symptoms and combating them with carbohydrate Reactions are particularly apt to occur following muscular exertion, and this demands either a careful regulation of exercise or the addition of extra carbohydrate at this time

The prodromes as well as the time of reactions differ from those occurring with regular insulin-reactions occurring usually 12 to 24 hours after the insulin has been injected. The usual symptoms of shock which are due to the protective mobilization of epinephrine are less pronounced The sugar level falls so gradually that the adrenal glands are not aroused-thus tremor, sweating, tachycardia, and a pounding pulse may be missing, and the symptoms of cerebral origin, such as drowsiness, headache, nausea, and fatigue, may be the only criteria of hypoglycemia. This adds to the confusion because these symptoms are not unlike those of diabetic acidosis It is important also to realize that reactions following protamine insulin are apt to be prolonged or even recur following the administration of glucose as more of the suspended insulin is liber-It is well, therefore, to instruct patients having reactions to take small amounts of sugar every 15 or 20 minutes until the next meal Severe reactions may occur at night, and it is not uncommon for the patient to awaken in the morning with sore and stiff muscles or even with a bitten tongue as a result of convulsions through the night.

It is not uncommon to note large subcutaneous swellings at the site of injection of protamine. These usually tend to disappear but it is even more important with protamine than regular insulin to vary the site of injection. Cases of atrophy of subcutaneous tissues have been observed following its use. E L Bortz (personal communication).

Dosage of Protamine Insulin-The average patient requires a smaller number of units of protamine today than he does of the older insulin, but as we have previously stated protamine is rather slow to reach its full effect, and in shifting to it from regular insulin many authorities prefer to administer small doses of regular insulin for a day or two until protamine is able to pick up the duty of caring for the blood sugar Wilder (ibid) has found that the substitution can be made fairly satisfactorily if four-tenths of the previous dose of regular insulin is administered the first day as a supplement and two-tenths of the previous dose on the second day Later the number of units of protamine insulin can usually be reduced. W A Fletcher, and R Campbell, A Kerr¹⁰ recommend giving 75 to 100 per cent of the previous dose of regular insulin as protamine in a single morning dose, accompanied the first day with about 60 per cent of the previous dose of regular insulin and on the second day with 30 per cent

Protamine Insulin in Acidosis and Surgery — Protamine insulin has been used infrequently in the treatment of diabetic acidosis as well as in the pre- and post-operative care of the surgical diabetic Wilder (ibid), A. F. Fowler E. H. Bensley, and I. M. Rabinowitch 11

In spite of apparently satisfactory results by these four investigators it would seem preferable in the vast majority of cases of this type to use regular insulin because it is important to obtain as prompt an insulin effect as possible in acidosis, and in both conditions to be able to control the height of the blood sugar within a short period of time which can certainly be accomplished more readily with regular insulin

While protamine insulin offers a great advance in the therapy of diabetes it is important to realize that no miracle has been accomplished by its introduction The basis of treatment is still diet, and while the newer insulins will in many cases result in a decreased number of injections in a sizeable proportion of cases they offer no advantages over the older insulm. It is well also to remember that many cases of diabetes do not do well with the slow-acting insulins, and approximately 25 per cent of cases in which protamine was used have been returned to regular insulin. It is impossible to anticipate which cases will do well with protamine, and certainly any patient taking multiple doses of insulin is entitled to a trial on the newer in-It is difficult in many cases to properly gauge the dose required and very often the optimum time of injection is one of marked inconvenience to the patient, and many cases will voluntarily be asked to be returned to the older msulms

Crystalline Insulin

Saehund (personal communication) crystallized insulin and found that a solution of it had a reaction that was considerably prolonged as compared with ordinary insulin. This preparation contains 0.9 mg of zinc per 1000 units

This insulin has a prolonged action, not quite as long in duration as prota-

mine, but gives a more prompt response in the sugar curve. Crystallized insulin is a clear solution, and in the experience of the author has proven very satisfactory. In cases of severe diabetes it can be given twice a day, but because of the duration of its action, it may be taken by the clock and not in relation to meals. It seems less apt to give severe reactions than does protamine. This insulin at the present time is not available for general use. It may be before the end of 1938.

Exercise in Diabetes

A. Marble and R M Smith¹² found that in the fasting diabetic, whose disease was well advanced and who had received no insulin for several hours, the immediate result of strenuous exercise was that of raising the blood sugar level. They feel that exercise apparently stimulates the breakdown of glycogen in the liver, with the resulting outpouring of sugar into the blood stream. It is probable that this increase in blood sugar may be attributable in part to an increased activity of the renal gland, caused by exercise.

The diabetic of today should lead an essentially normal life, with an average amount of activity. If the diabetic condition is imperfectly controlled and if the body has been supplied with an madequate amount of insulin, exercise, instead of conferring a benefit, may actually increase the hyperglycemia and glycosuria For exercise to exert its maximum effect, sufficient insulin should be available in the body at the time of exercise They point out that as the diabetic arises in the morning, the logical sequence of events should be insulin, exercise and breakfast, rather than exercise, insulin and breakfast. The exercise should be moderate enough so that undue fatigue is not produced

Complications of Diabetes

I. O. Piper¹³ discusses coma, neuritis, infection, gangrene, arteriosclerosis and associated heart degeneration as the complications of diabetes mellitus Diabetic coma must always be considered an emergency and treated as such Before the use of insulin it was almost 100 per cent fatal and since the use of insulin it is almost 100 per cent curable if handled properly The diagnosis of diabetic coma is established by always finding the blood sugar elevated to a high degree and the combining power of carbon dioxide decreased markedly Neuritis is a troublesome complication of diabetes There is no special treatment for this condition, except to control the diabetes in the best possible manner The neuritis may persist for a long time after the diabetes is under control, but recovery almost always occurs There is little evidence to show that diabetes is caused by infection but a great deal of evidence that it is made worse by it, in fact, mild diabetes may be turned into a very severe form of this disease. Infections are very prone to occur in the diabetic patient and advance rapidly Hence a vicious circle is set up diabetes is made worse by the infection and the infection is aided by the diabetes In treating these infections this vicious circle must be broken and the best way is to incise freely all pus pockets and institute free drainage. The best known treatment for infection in the known diabetic patient is prophylaxis, by teaching the patient the proper hygiene of all parts of the body. The several types of gangrene in diabetes are the arteriosclerotic, obliterative endarteritic, embolic and obliterating thrombo-anguitic and diabetic. The diabetic form is distinctive from the others in that the gangrene spreads laterally as well as along the vessels or line of circulation

Circulation is always interfered with in these cases. Then if a very slight infection takes place, which may come from as small an injury as a cut on the toe from trimming the toenail, gangrene is apt to set in Sometimes the infection seems to come from within Conservative treatment can be carried out only on the diabetic gangrene, and this is probably successful only in the early cases Conservative treatment does not offer much in the first three types of gangrene The mortality of amputation cases is fairly high. Most of these patients die from septicenna and bronchopneumonia. Joslin states that the average span of life after amputation is two vears. He believes that arteriosclerosis is secondary to diabetes and that the duration of the disease is an important factor in the production of it. He found that diabetes of a duration of five years or longer is practically always complicated by arteriosclerosis. It has been shown that arteriosclerosis progresses in the diabetic patient in spite of the proper treatment with diet and insulin Every diabetic patient should receive a searching examination, especially relating to the condition of the heart muscle and for coronary damage. Distinct damage may be done by the use of insulin in the treatment of these cases, and death may ensue in some of them

Coma—H Walker 14 reports his experience in 108 consecutive cases of diabetic acidosis seen at the Mayo Clinic, and stresses the connection of abdominal pain as an important symptom. This has been previously expressed by McKittrick Beardwood, and others. Walker feels that this is due entirely to the level of blood chlorides, and found prompt relief when sufficient salt was administered.

E S Dillon, H E Riggs and W W Dyer¹⁵ examined the brain in eight fatal cases of uncomplicated diabetic coma and

observed dilatation of the capillaries, perivascular edema, proliferation of the neuroglia and degeneration of the ganglionic cells These abnormalities were most conspicuous in those parts of the brain which have been shown to be most susceptible to anoxemia produced by acute exsanguinating hemorrhage or by heart Furthermore, the lesions were like those noted after acute asphyxia In diabetic coma the total volume of the blood is reduced by hemoconcentration to a degree comparable to that in severe hemorrhage, and severe myocardial damage frequently accompanies it Thus, it seemed to the authors that the abnormal physiology of diabetic coma is a reduced volume of circulating blood, a consequent marked reduction of blood pressure, both systolic and diastolic, limitation of the amount of blood flowing to the head and resulting anoxia of the brain. The cerebral lesions, in turn, may further embarrass the cardiac function by paralysis of the vasomotor and other vegetative centers, and in consequence the patient may die as a result of collapse of the vasomotor system or failure of the respiratory function, even when chemical estimation of the degree of acidosis indicates an improvement

The Electrocardiogram During Diabetic Coma - Certain observations suggested to S. Bellet and W. W. Dyer¹⁶ that rather marked and, on the whole, consistent alterations of the T-waves and lengthening of the QT interval were present during certain stages of diabetic coma after the acidosis had been partially or completely controlled. This led to the observation of 17 cases of diabetic coma and six cases of "precoma" Electrocardiographic changes were observed in every one of the cases studied by serial electrocardiograms during and on emergence from diabetic coma The electrocardiographic changes of the coma cases were graded as severe in eight, moderate in six and slight in three; the electrocardiographic changes in the six precoma cases were similar, although less severe than were the changes of those patients who entered the hospital in coma Only one showed severe electrocardiographic changes, four showed moderate and one slight changes The chief alterations observed were lengthening of the QT interval, depression of the ST interval and inverted T-waves Alterations in the QRS complexes were infrequent all except three cases of the entire series of diabetic acidosis the electrocardiogram eventually returned to normal The most abnormal electrocardiographic changes were observed not during coma but about 24 hours later when the patient was clinically improved and out of the acidotic state Serial electrocardiographic studies may be an important method of gauging the severity of cardiac disturbance during and on emergence from diabetic coma

Circulatory Complications of Diabetes Mellitus - P Radnai and R Weisz¹⁷ direct attention to the circulatory complications of diabetes mellitus Their observations were made in 400 Electrocardiographic tests were made in 260 of these and it was found that 40 per cent showed changes Cardiac decompensation was discovered in 20 per cent, anginoid conditions in ten per cent, vascular changes of the fundus oculi in 30 per cent and peripheral arteriosclerosis in eight per cent. It was observed that the electrocardiographic changes as well as the appearance of cardiac disorders are primarily dependent on the age of the patient and secondly on the height of the blood sugar Insulin therapy or the quantity of insulin seems to be of no importance in the development of cardiac disorders was impossible to prove that diabetes mellitus is a causal factor in hypertension. The cardiac disturbances of diabetic patients are not caused by the hypertension that may exist but rather by the metabolic disorder that accelerates and increases the development of vascular changes. Besides the age of the patient it is chiefly the blood sugar value and the duration of the metabolic disorder that influence the development of The degenerative cardiac disorders. processes in the fundus oculi are the result of the metabolic disturbance Their development, too, aside from the age of the patient, is dependent chiefly on the height of the blood sugar and the glyco-The author emphasizes that a thorough clinical examination of a diabetic patient requires not only an exammation of the urine and the blood but also an inspection of the retina and an electrocardiographic test. In case of pains in the extremities, an oscillometric examination is necessary Oscillometric changes and the appearance of symptoms of peripheral arteriosclerosis are dependent on the age of the patient and on the duration of the metabolic disorder. If the blood sugar is unusually high, cardiac and retinal disturbances predominate but peripheral arteriosclerosis appears generally in those persons in whom the metabolic disorder is one of long standing but in whom the blood sugar is comparatively low so that insulin is given either in small doses or not at all

Diabetic Arteriosclerosis — By injecting metallic mercury into the pophieal artery and taking roentgenograms of the entire leg below the knee, T. A. Henderson¹⁸ has studied the gross pathologic changes in the arterial channels of seven diabetic legs which have come to amputation. The mercury was introduced at approximately systolic blood pressure, so that a rough approximation of physiologic conditions was produced. As

metallic mercury will not pass through capillaries, a clear picture of the available arterial channels in a given leg can be obtained After a study of the roentgenograms the leg was dissected at strategic points and the arteries were studied directly. The order of involvement of the arteries seemed to be posterior tibial, peroneal and anterior tibial. The extent of the arterial changes corresponds much more to the duration of the diabetes than it does to the age of the patient It seems possible that diabetic arteriosclerosis starts as a patchy affair. It may sometimes occlude a major vessel so rapidly that adequate collateral circulation cannot develop to prevent gan-It may sometimes progress slowly, accompanied by the development of good collateral circulation, and eventually involve most of the major vessels in a diffuse process. At this stage it either resembles or is identical with nondiabetic or senile arteriosclerosis. In the slowly developing cases the collateral vessels, though never able to deliver a normally rich supply of arterial blood to the part, seem often to be sufficient to keep the patient symptom-free or to diminish only slightly his activity and comfort if infection is avoided Infection seems to be the precipitating factor

Diabetes and Tuberculosis—D M Dunlop¹⁰ suggests that the liability of patients having severe diabetes to develop tuberculosis should be constantly kept in mind. The possibility of this complication having occurred should always be suspected and excluded when, for no obvious reason, a previously controlled diabetic patient begins to require larger doses of insulin, to lose weight and to fail in general health. The danger is particularly present in patients who have suffered from hyperglycemic coma and in diabetic children. Such cases should be examined at intervals for the

specific purpose of excluding tuberculosis, young diabetic patients should be particularly excluded from association with open cases of tuberculosis. With early diagnosis of the tuberculosis and efficient treatment of the diabetes there is no reason to believe that diabetes will have an adverse effect on the tuberculous process. A high caloric, high fat, low carbohydrate diet with sufficient insulin should be used, and, if the case is otherwise suitable, artificial pneumothorax should be induced under sanatorium conditions whenever possible

Amenorrhea in Diabetes-R Bompiani²⁰ says that amenorrhea and the development of involutive changes of the genitalia in diabetes are secondary to alterations of the anterior lobe of the hypophysis and of the diencephalon By reviewing clinical and experimental reports in the literature it is obvious that the anterior lobe of the hypophysis and the hypothalamic nuclei are the structures by which the sugar metabolism and the phenomena of the uterme-ovarian cycle are controlled. On the one hand, hypophysical syndromes are frequently associated with changes in the sexual function and alterations of the genitalia and, on the other hand, anatomic alterations of the hypophysis and of the diencephalon are often found in diabetes of definite insular origin. According to the author, the hypophyseal-hypothalamic pathogenic mechanism of amenorrhea explains the frequent production of amenorrhea preceding diabetes and the re-establishment of the uterine-ovarian cycle and the regaining of fecundity in women suffering from amenorrhea and treated with insulin

Causes for Failure in Treatment of Diabetes

R W Finley²¹ divided the treatment of diabetes into three parts

- 1. To clear up or prevent the immediate symptoms of dextrose deprivation, such as glycosuria, dehydration, malnutrition and the profound cellular chemical changes antecedent to and productive of severe acidosis and coma
- 2 To guard the patient against considering his diabetes a threat against his self esteem
- 3 To help the patient evolve a plan or pattern of dietary and therefore of social and work conduct, which he is willing to follow and which gives most promise of avoiding the development or the advance of arteriosclerosis

These three objects run concurrently and are best begun at the first conference with the patient Undernutrition must be avoided and a hyperglycemia alone or a glycosuria alone cannot be accepted as a trustworthy evidence of the condition Attempts to keep a patient on a diet too low in nutritional value in order to clear the urine of sugar when the blood sugar is within acceptable limits, to keep a blood sugar at some conventionally accepted normal level when the kidneys are not leaking sugar or to avoid the use of insulin cannot be accepted as the best medical practice, because it may be using a state of undernutrition as the means to treat a chemical change Persistent glycosuria, when present with persistent hypergly cemia, is bound to lead sooner or later to undernutrition and must be cleared if possible Chycosuria in the absence of a chronic focus of infection is due to a delayed absorptive activity of the tubules of the kidney, which returns the sugar from the glomerular urine to the blood The logical treatment seems to be to allow a diet which yields enough dextrose to supply both that lost in the urine and that needed to maintain a normal state of nutrition, and then to follow the blood sugar more frequently than would be called for otherwise in order to be sure that the glycosuria and a hyperglycemia are not occurring together

Diabetes Mellitus, Gall Bladder and Obesity

A Terbruggen²² decided to make a statistical analysis of a necropsy material with regard to the connection existing between age, obesity and diabetes mel-In diabetic patients of less than 50 years of age, he never noticed a combination with cholecystopathy. In diabetic patients between the ages of 30 and 50, obesity was comparatively frequent and in those beyond the age of 50 it was extremely frequent. The author thinks that the concurrence of diabetes with gallstones is not so frequent as to suggest a casual connection with diabetes mellitus, thus there is no reason to regard diabetes mellitus as a sequel to biliary disease The author explains the concurrence of biliary disorders and diabetes mellitus as the result of obesity. which occurs in both conditions suggests that on the one hand obesity favors the development of biliary disorders, and, on the other hand, in case of a predisposition, it also leads to the manifestation of diabetes mellitus

Causes of Death Among Diabetic Patients

B von Bonsdorft²³ says that from 1930 to 1936 308 diabetic patients (117 men, 191 women) were treated in the Maria Hospital in Helsingfors, most of them several times, 110 were less than 50 Of these, 120 have died, at an average age of 565 years, 508 per cent from arteriosclerotic cardiopathies and cerebral circulatory disturbances together with gangrene in the lower extremities, 158 per cent from infectious diseases, 143 per cent from diabetic coma, ten per cent from tuberculosis and 58 per cent from malignant tumors. At least 65

cases of coma (in 45 patients) were treated; of the 17 deaths in this group, some might have been prevented if the cases had not been admitted too late because of mistaken diagnosis.

Insulin Atrophy

According to M. Rosenberg and F. Berliner,24 Depisch was the first to describe, in 1926, local disappearance of fat in diabetic patients on insulin treatment Depisch named it "insulinlipodystrophy." The one observation reported in common by several authors was that the lesion occurred much more frequently in women than in men Two possibilities were advanced as to its etiology One was that of a specific as vet unexplained hormone action of insulm, and the other that of a chemical or traumatic damage of the act of injection Graham and Carmichael believed that a certain amount of the lipolytic ferment in the insulin, because of its derivation from the pancreas, was responsible for the local fat necrosis. The presence of such a ferment in the insulin, however, was not demonstrated. Avery believed the necrosis to be the result of a long-continued local inflammatory process resulting from injections. This view was not confirmed by histologic studies. The authors in their study of the subject found that among 4000 diabetic patients treated on insulin therapy the incidence of local fat atrophy was less than 0.5 per cent. The predisposition of the part of the female sex was marked There were 27 of the female and five of the male sex. The age of the patient and the duration of diabetes played no part in the incidence. Duration of the injection treatment, however, was an important factor. Fat atrophy was not seen in patients who received injections less than three months. In a study of 1000 consecutive patients ad-

mitted to a dispensary, the authors observed the same phenomenon in four nondiabetic patients and in one with mild diabetes. None of the five received injections of any kind Four were women In three the area of dystrophy on the thigh came in contact with the rim of a tub in which the patients did their daily washing of clothes Because of a similar frequency in the groups and the clear evidence of trauma in the second group, the authors are inclined to ascribe the phenomenon of local fat atrophy to oftrepeated trauma rather than to some local or general effect of insulin

Lipomatosis in Insulin-Injected Areas

G B Bader and F Vero²⁵ report their case of lipoma-like masses in a diabetes mellitus for 414 years. His diet was high in carbohydrates and low in The disease has been fairly well controlled with two injections of insulin daily one before breakfast and one be-The insulin requirements tore supper per day have varied between 50 and 80 units during the last two years blood cholesterols have varied within normal limits. Two years ago very small swellings were noted in the insulin-injected areas Both biceps, both buttocks and the anterior aspect of both thighs These swellings were described as localized edematous symmetrically distributed tumefactions. In spite of the admonition to avoid these areas in the tuture, the patient continued to use them for insulin injections because "it hurt less" when these areas were used. As a result of the continuous use of these areas, the swellings have increased steadily in size These sections show a moderate hyperkeratosis with edema of the epidermis, portions of which appear to be slightly atrophied The corium is somewhat edematous, the site of a slight chronic inflammatory reaction There appears to be a moderate fibrosis of the corium The principal feature, however, is the attached adipose tissue, which is composed of very large cells and shows evidence of encapsula-The adipose tissue comes fairly close to the epidermis in one place, and within it one sees a hair follicle and a smooth muscle bundle, as is frequently the case when the skin atrophies No serious sequel has been observed so far, and the lipomatous process seems to be benign No therapy has influenced them. but a definite reduction in size can be noticed when further injections in the area are avoided.

A very complete survey of this condition is reported by J A Shelly26, in which he feels that possibly the insulin atrophy is due to some acceleration in the metabolism of the tissues

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OBESITY

The concept of the etiology of obesity has changed little during the past five or six years except that there seems to be a tendency to appreciate more and more the place of hyperalimentation in its production both in those cases which have been labeled simple obesity, as well as those thought to be due to endocrine disturbance H R Rony¹ speaks of the high incidence of obesity in diabetics He points out that the frequent occurrence of these two conditions together has led to the presence of a low sugar tolerance in obese persons, to be regarded as a danger sign of diabetes This prognostic evaluation is the more conspicuous as low sugar tolerance in other clinical conditions is, as a rule, not thought to be conducive to diabetes He has had 20 obese patients with low sugar tolerance under observation for from one to nine years in order to find out when and under what conditions manifest signs and symptoms of diabetes would appear None of them developed diabetes. As the patients received instructions to follow a low caloric diet, one might think that the undernutrition was instrumental in preventing the development of diabetes However, at least six of the patients failed to restrict their food intake It appears therefore that low sugar tolerance observed in obese persons is not, in itself, indicative of a danger of diabetes. In this respect low sugar tolerance in obesity does not seem to differ from the low sugar tolerance observed in other conditions. However, there is a notable difference between obese persons with low sugar tolerance and normal persons: The former invariably show a marked improvement of their sugar tolerance, while the latter are known to respond with a marked decrease of sugar tolerance The author suggests that this peculiar difference may be due to the rôle of the fat tissue in blood sugar regulation During the first three hours following a dextrose test meal, dextrose accumulation in tissues other than the liver constitutes the major mechanism of blood sugar regulation There is uncontested evidence that among other tissues the fat tissue may prominently participate in the mechanism of blood sugar removal after dextrose ingestion Previous undernutrition tends to make the fat tissues capable of absorbing large amounts of sugar from hyper-The basic effect of glycemic blood undernutrition on carbohydrate metabol-1sm-be it to decrease insulin sensitiveness or something else-may be the same in normal as in obese persons. In individuals with small amounts of fat tissue, this effect appears in the form of decreased dextrose tolerance. In persons with large amounts of excess fat tissue the same effect is compensated by accumulation of carboly drate in the fat tissue, with the result that the blood sugar time curve becomes flatter, giving the picture of improved dextrose tolerance

Obesity in Children

The subject of obesity in children has been greatly neglected by most investigators, and it is of interest to read that P. Mallam² is convinced that dieting is

the keystone to treatment in almost all cases of obesity in children, but before prescribing a system of diet a careful family history and knowledge of conditions under which the child is being reared must be obtained. Obesity beginning in childhood often gives rise to endocrine trouble later on, and when one finds a strong dominant obesity factor in the family one should always be prepared to face a more difficult task than in a purely fortuitous case arising from normal stock Even then, however, a cure, permanent and complete, can be obtained in the majority of cases by simple measures The treatment must be explained carefully to the child and need not be elaborate. A simple practice is to weigh and measure the child and give it a diet based on the calculated basal requirements for this particular height and size. This is merely a beginning figure, and it may be necessary either to add to or subtract from the initial starting point. The question of the fluid intake is of considerable importance. If these children are counseled to drink early in the morning and then to try not to drink at all through the day, this is often a great help in reducing weight Appetite is largely a question of satiation and these children must be schooled to eat slowly. Salt and sugar should be cut down to a minimum. Many children appear even tatter than they are because of postural defects. Exercises devoted to training the recti abdominis and correcting any possible lordosis and to making them stretch their overloaded limbs are all valuable. Such exercises are always more effective under trained supervision and are usually better done in a class of several children Some sort of abdominal support employed temporarily often gives considerable help. At the same time strengthening exercises are absolutely essential, for without them one

must either rely on artificial means or face a serious chance of visceroptosis. If a child loses weight consistently under treatment, the treatment is being overdone. If one treats an overweight child of ten years and at 12 the child weighs the same, one should realize that a great deal has been achieved

Obesity in Adults

W J Kerr and J B Lagen³ discuss a type of obesity that appears to be exogenous in origin, arising in persons whose dietary habits lead to a caloric intake beyond their daily requirements It is not easy to determine whether individuals with the relaxed habitues are predisposed to the train of events which follow, but it is apparent that, when medical attention is sought, these patients present the posture of relaxation The gradual accumulation of adipose tissue in the normal depots for fat gives the appearance of rotundity usually designated as corpulence The accumulation of fat in the third decade is relatively symptomless. In the fourth decade the appearance of the individual is one of increasing corpulence, with a tendency toward a florid complexion. The normal curves of the spine are accentuated. The added weight of fat of the abdominal wall and viscera moves the line of gravity forward, and to compensate for this the major portion of the thojax is moved backward, accentuating the lumbar curve The upper part of the thorax and shoulder girdle move forward, increasing the normal thoracic curve, and the head and neck are thrust forward as is required for adjustment at a new line of gravity The fifth decade marks the period of transition from the state of physical well being and activity of youth to one of gradual lessening of activity of middle and old age The syndrome itself is certainly modified or delayed in susceptible individuals by proper exercise and diet Heredity may be a factor in its development, as shown by the familial occurrence of arteriosclerosis, arthritis, premature grav hair and particularly corpulence Environment is related directly The condition singles out individuals of sedentary occupation. The most obvious result is the gradual development of a heavy, pendulous abdomen The respiratory and circulatory manifestations are primarily due to interference with proper ventilation of the lungs based on postural defects and the disadvantages under which the diaphragm functions under the circumstances The orthostatic dyspnea, reduced vital capacity and tidal air, polycythemia and cyanosis are closely related In older subjects hypertension, systemic and pulmonary, and arteriosclerosis account for definite cardiac complications Treatment requires temporary support for the pendulous abdomen and assistance in the evacuation of the lungs during expiration A belt gives this support and aids in expiration. The weight should be gradually reduced to correct the distortion of the spinal axis and restore the spinal curvature Postural training is of greater value after the adipose tissue has been reduced but is of little value in the patient with a pendulous abdomen and a great counterweight of visceral fat that interferes with the ascent of the diaphragm during expiration

H Coombs, D Reader and C Catlin⁴ stresses the importance of diet in the control of obesity. Without some control of the diet, all other methods are likely to fail. The few contraindications to treatment by means of dietetic control include extreme old age, acute disease (tonsillitis and rheumatic fever) and severe disease (grave anemia), and when fainting, nervousness, weakness or irritability occurs the treatment should be interrupted for a

short period. Medical supervision should be insisted on throughout the entire treatment, and, if possible, for some time afterward so that the patient may be kept at the optimal weight. The scientific principles consist of (1) restriction of carbohydrates, more especially of the concentrated forms, such as sugar, bread, potatoes, beer and ginger beer, (2) restriction of fats that do not contain vitamins, (3) very little restriction of proteins, (4) a generous supply of vegetables and fruit to provide bulk and to satisfy hunger, (5) an adequate supply of vitamins by vegetables, fruit, eggs, milk and butter, (6) an adequate supply of minerals by salads and milk and restriction of table salt, (7) no restriction of fluids, (8) bulky meals, to prevent hunger, and (9) three or four meals during the day but nothing between meals Another fundamental method of attacking obesity is by the inauguration of proper exercise. Patients must be encouraged to increase their activity gradually, and dancing, swimming, walking, and golf are particularly to be rec-Unlike diet and exercise. ommended glandular therapy is not without considerable danger Thyroid medication often causes addiction and predisposes a patient to thyrotoxicosis and auricular fibrillation The administration of drugs (nitrophenols) should be used with the greatest caution and only by those fully aware of its dangers Occasionally, surgery is necessary for the removal of fatty tumors, and the surgical removal of adipose tissue in the abdominal region is The adiposity sometimes undertaken generally does not recur in the same region, but this method of treatment is illogical and commands no widespread approval Physical therapy is a useful adjunct to the treatment of many diseases and obesity is no exception, but there is considerable truth in the state-

ment that the only person who loses weight by massage is the masseuse **Baths**, **diuretics** and **purging** should be employed only under medical supervision. The results of treatment depend a great deal on the education of the patient and the personality of the practitioner. The dangers of obesity should be explained and the rationale of the therapeutic measures given consideration.

The most startling and possibly romantic development in treatment of obesity was the introduction of dinitrophaneal three years ago. This drug gained rapidly, wide clinical use and unfortunately wide notoriety because of some of its untoward effects.

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VITAMINS

Vıtamin A

The publication, in 1934, of a clinical method of determination of vitamin A deficiencies using a photometric technic (Jeans et al.), and recent chemical advances have stimulated new interest in this field Crystalline vitamin A has been obtained by Holmes and Corbett and Fuson and Christ have reported synthesis. As yet these products are not available commercially

Pathology—According to S B Wolbach² the primary effect of vitamin A deficiency is on epithelial structures resulting in atrophy and substitution of a stratified keratinizing epithelium identical in all locations and arising from focal proliferation of basal cells. This process may be called keratinizing metaplasia. The gross pathologic lesions result from

accumulation of keratinized epithelium in glands and ducts In the lung, for instance, cyst formation, bronchial occlusion, bronchiectasis and atelectasis may occur These conditions may favor infection, giving rise to the previous belief that vitamin A was anti-infective in action. In the rat, metaplasia is seen first in the salivary glands followed in order by the respiratory tract, genitourinary tract, and eye In humans as well as in experimental animals keratinizing metaplasia occurs in the eye in a late stage of deficiency. There is evidence that vitamin A is important to the proper development of teeth in the infant Secondary effects of vitamin A deficiency are loss of weight due to loss of fat and muscle wasting, anemia, cessation of growth of bones, degenerative lesions of skeletal muscle and lymphoid hyperplasia of the spleen Hemosiderin is frequently deposited in liver and spleen

Regeneration of tissue begins on administration of the vitamin and differentiation of surface epithelium appears

Chemistry and Physiology — H Jeghers3 has reviewed the present knowledge of vitamin A Dietary vitamin A comes from carotene or carotenoid substances, and vitamin A of animal tissues Humans are unable to synthesize either carotene or vitamin A Carotene is a crystallizable hydrocarbon related to the terpines, while vitamin A is a primary alcohol derivative of one-half of the carotene molecule Being fat soluble both are absorbed by the lacteals of the intestine and enter the blood through the thoracic duct No change occurs in the process Carotene is changed to vitamin A in the liver by an enzyme called carotenase Fever, rapid growth, infection, elevated B M R and pregnancy all increase the need of vitamin A, while lack of bile or pancreatic secretion, changes in the gastrointestinal mucosa and disturbances of motility of the gastrointestinal tract all prevent or hinder the proper absorption of this vitamin. Liver disease prevents proper storage of vitamin A as well as the conversion of carotene to vitamin A. Any of these mechanisms may result in vitamin A deficiency even with a theoretically adequate diet

Sources—The best sources are Cow's

ening of skin, papular cornified lesions about hair follicles more on extensor surfaces and shoulders; loss of weight; genitourinary infections, kidney stones(?)

Tests of Deficiency — Photometric determinations are based on the conception of Wald that vitamin A combines with protein to form visual purple which is broken down by light into a

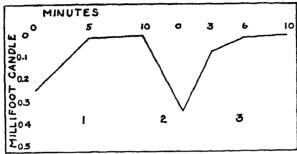


Fig 1—Plotted readings of a test of a normal subject 1, foreperiod, 2, light period, 3, recovery period

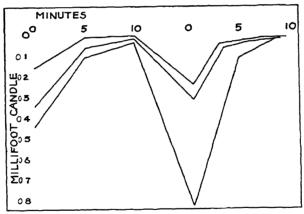


Fig. 2—Test results showing improvement obtained in 10 and 16 days respectively with 20 000 units of carotene duly

milk, human milk, eggs, animal livers, cod-liver oil, cheese, butter Good sources are Spinach, watercress, carrots, green peas, lettuce, oranges, tomatoes

Symptoms—Eye Night blindness, dryness of conjunctiva (xerosis) with Bitot's spots (foam or frost), decreased tear secretion, keratomalacia, meibomatis, blepharitis, hordeolum, edema and puffiness of lids General Bronchitis, bronchopneumonia, bronchiectasis, sinusitis, hoarseness, dryness of skin, rough-

be reformed to visual purple or transformed to visual purple or transformed to visual purple or transformed to visual. A to start the cycle over again. Some vitamin A is lost in the process and must be replaced by the diet. Lack of replacement may be measured by the inability to see in dim light. A person may show normal vision by the usual tests and yet give abnormal results in dim light. Blanching of the visual purple by bright light creates a greater demand for vitamin A, and a de-

ficiency of this vitamin results in prolonged blinding effects of bright light. P. C Jeans, E Blanchard, and Z Zentmire⁴ have devised a new instrument for measuring the degree of night blindness called the *biophotometer* and have modified the technic described in 1934. They suggest the following. (1) Ten minutes in the dark, (2) exposure to bright light of photometer for three minutes; (3) ten minutes in the dark the presence of adequate vitamin A Recovery occurs following administration of vitamin A to deficient persons and is indicated in Fig. 2

Low normal limits are stated to be about 0.6 millifoot candles of light. The authors believe that, if the technic is carefully followed, the range of experimental error is not great enough to interfere with interpretation. J. B. You mans, M. B. Corlette, H. Frank and

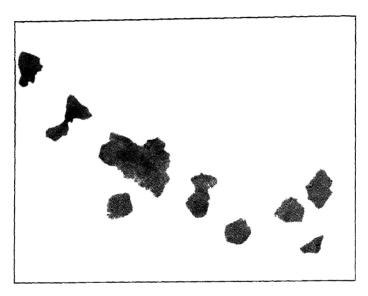


Fig. 3—Smear from the bulbar conjunctive of a white housewife aged 52, who complained of vigue pairs in the irms poor vision pain and burning in the eyes and slight photophobia. There is marked connitication of all the cells

Readings are made at the beginning, middle and end of the foreperiod and at the beginning and end of the recovery period with one or two additional readings during the recovery period. If the readings obtained are plotted according to millifoot candles of light against time a rather typical curve is obtained.

The first readings after the exposure are the most informative since they give an indication as to rapidity of regeneration of visual purple after blanching with bright light. A rapid recovery indicates ample vitamin A supply. There are individual variations, however, even in

M (r Corlette, after testing 54 healthy adults and 50 adult outpatients found the initial recovery readings in 83 per cent of the former group were 0.7 millifoot candles or less, while 50 per cent of the patients showed poorer readings. All subjects showing poor response who were given large doses of vitamin A for four to six weeks showed improvement up to 0.7 millifoot candles. Youmans proposes this reading as a tentative normal for adults

A method of studying infants for vitamin A deficiency has been described by C Friderichsen and C Edmund ⁶ It is

based on determining the faintest light to which a child reacts when his eye is maximally adapted to darkness. It was found that in normals there was a minimum of light irritant that would result in typical reflex movements. This "minimum reflexible" is quite constant for any given child and is dependent to a large extent on normal vitamin A content, according to this writer. The minimum reflexible as determined in 106 infants

method for which was described by F. H. Carr and E A. Price¹⁰ in 1926, using antimony trichloride and a Lovibond tintometer W. Stepp and H Wendt¹¹ report a series of readings of carotene and vitamin A in healthy men in Lovibond units. It was found that the level of carotene was 26 times the vitamin A level in July, and higher in October. In certain pathologic conditions there was an alteration in figures and ratio;

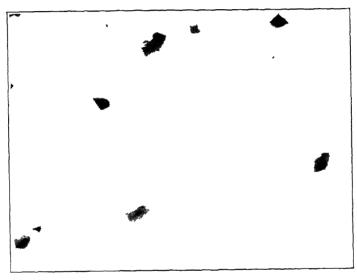


Fig 4—Smear from the same patient as in Fig 1 after two weeks' treatment with cod-liver oil. Many of the cells now are nucleated and show a return toward normal. (Courtess. Jour. A. M. A., Jan. 2, 1937.)

was found to be six as measured by Tscherning photometric lenses. The necessity of using stronger light was thought to indicate vitamin A deficiency and could be made normal by administration of vitamin A.

Another method of determining vitamin A deficiency consists of the study of scrapings from conjunctiva of nose Cormfication or keratimidation of the cells indicates deficiency 7, 8 J B Youmans has recently published photomicrographs of such changes

Recent attempts have been made to obtain information from blood serum, a

in hypothyroidism there seems to be impairment in transformation of carotene to vitamin A resulting in a high ratio, in chronic liver diseases both carotene and vitamin A were decreased while in acute hepatitis normal or increased values were found

Incidence of Deficiency—In a recent series of investigations Jeans, et al (ibid), found 35 per cent of orphanage children and 19 per cent of local school children showing abnormal curves. H Jeghers 12 has studied adults by means of the photometer. In his first report 274 persons were tested. Three groups were

represented I House officers, II W. I' A workers, medical students, technicians, graduate nurses, III Ambulatory patients The results may be tabulated as follows

| | Cases | Degree of Deficiency | | | | |
|----------------------------------|------------------|-------------------------|------------------------------|---------------------------------------|----------------------|--|
| | | Normal | Mild | Mod- erate | Se- vere | |
| Group I Group II Group III | 22 149 103 | 91 0% 65 8% 33 0% | 9 0° c 28 2° c 41 7° c | 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 | 0 0% 1 4% 7 7% | |

In a subsequent report, Jeghers¹³ studied 162 students, obtaining photometric readings and detailed dietary histories. Evidence of deficiency was found in 35 per cent. In order to evaluate the importance of deficiency in producing photometric changes, 50 students showing the best dark adaptation were compared with 50 showing the poorest response. Table 1 compared the dietary habits of the two groups.

Clinical data on the two groups showed that colds were not more frequent but were more prolonged in the deficient group. Focal infections, night blindness, photophobia, dryness of the conjunctiva, burning eves, blephantis, dryness of the skin, hyperkeratosis tollicularis and itching skin were more frequent in the deficient group. The average daily intake of vitamin A in the normal group was calculated to be 5560 international units, while in the subnormal group the average daily intake was calculated as 2445 international units.

The deficient group was treated with vitamin A as carotene in oil or halibut liver oil concentrate. The best results were obtained when 70,000 units of vitamin A were given orally per day for two weeks followed by 25,000 units daily until adaptation became normal. The therapeutic results were striking, both objectively and subjectively

Requirements - Jeans, et al (loc cit), concluded from a limited number of tests in children that the minimal requirements were about 3000 units of Jeghers (loc. cit) vitamin A daily concluded from his observations that 4000 units is sufficient to maintain normal dark adaptation but feels that 6000 units would be a safer optimal level for healthy adults The latter author produced evidence of vitamin A deficiency in himself by a very deficient diet (200 units per day). The first photometric evidence appeared in six days and subjective evidence (night blind-Using a large ness) in five weeks amount of vitamin A (100,000 units daily) the photometric response returned to normal within three days

Vitamin B Complex

Since the isolation of crystalline vitamin B₁ by Williams and associates in 1934, and the synthesis by the same authors in 1936 there has been a great advance in the knowledge of its clinical importance Although originally termed the antineuritic vitamin because of its ability to prevent and cure polyneuritis, recent work has indicated an important relationship between this vitamin and metabolism There have also been developments in the knowledge of other fractions of the B complex including B, or G, B₆ and nicotinic acid Many of the fractions require further study before their clinical importance is understood.

Pathology—The advanced stages of B₁ deficiency have been so frequently described that further discussion of the syndrome of beriberr is unnecessary. The primary pathologic lesion seems to be a degeneration of the myelin sheaths of peripheral nerves. Wolbach (loc cit) believes that these nerve changes may be secondary and not necessarily char-

TABLE 1

EATING HABITS OF FIFTY PERSONS WITH NORMAL DARK ADAPTATION CONTRASTED WITH THOSE OF FIFTY PERSONS WITH SUBNORMAL DARK ADAPTATION

| | | | Sub- normal Group | |
|--|----|--|-------------------------|----------------------------------|
| Men Women Persons eating at home Persons cating at restaurants Persons cooking and eating in living quarters Average weekly amount spent by persons eating in restaurants Average weekly amount spent by persons cooking and eating in living quarters Persons eating three complete meals daily | 16 | 90° c 10% 74% 16° c 10% 7 00 4 20 32° c | 2 | 32% 26% 5 50 2 80 4% |
| Persons eating two complete meals daily Persons eating one complete meal daily | 34 | 68°° | 18 30 | 36° c 60° c |

(Courtesy Jour Amer Medical Assoc, Sept 4, 1937)

acteristic of vitamin B deficiency alone The rapid recovery from symptoms of polyneuritis seems to argue against demyelinization as being primarily responsible. These changes are associated with a disturbance in metabolism resulting in retention of lactic and pyruvic acids. Heart muscle, kidney tissue, and brain tissue have been found to give evidence of these changes in experimental animals (Kinnersley and Peters, Peters and Thompson, and Sherman and Elvehjem.) Tests in human beriberi have shown an increase in blood carbonyl compounds including pyruvic acid. (Platt and Lu.)

Vitamin B₂ or G has been the subject of controversy. Originally thought to be the antipellagra factor in the B complex, turther work has apparently proved it otherwise. The official name of this substance is now riboflavin ¹⁴. The exact importance of riboflavin is unknown except that it is necessary for growth and survival of rats (McCollum, loc. cit.) and recently lesions in the nervous system of dogs have been demonstrated by H. M. Zimmerman, G. R. Cowgill and J. C. Fox, Jr. ¹⁵. The earlier work of Goldberger seemed to indicate that vitamin G deficiency produced black

tongue in dogs, a condition thought to simulate pellagra in the human Zimmerman and his colleagues, however, from their experiments concluded that the Goldberger diet is probably deficient in other factors. In their animals on diets formulated by Cowgill and believed to contain all factors except vitamin G, a typical syndrome occurred manifested by slowly progressive loss of weight, vomiting, diarrhea, muscular weakness and death in 200 to 300 days Administration of liver extract as a source of G produced miraculous improvement Anatomic changes consisted of marked destruction of medullary sheaths of peripheral nerves, degeneration of medullary sheaths of posterior and less often anterior roots of the cord and degeneration of the medullary sheaths of the posterior columns with replacement by gliosis

Wolbach (loc cit) calls attention to another B fraction, B₆, a deficiency of which results in derinatitis in rats. This is probably not the antipellagra factor in humans. Its clinical importance is unknown

The possible importance of *nicotinic* acid in pellagra has been suggested by

C. A. Elvehjem, et al. 16. These workers have isolated from liver extract a crystal-line nicotinic acid amide which is highly active in the cure of experimental black-tongue in dogs. Synthetic nicotinic acid was also effectual. Nicotinic acid has been a known constituent of the B complex since the investigations of Funk 17 in 1911.

Symptoms—In view of the unsettled state of knowledge regarding the components of the B complex, the symptomatology of the various deficiencies in clinical medicine is uncertain. Loss of weight, anorexia, polyneuritis, central and peripheral nervous lesions, impaired intestinal function, impaired metabolic functions, have all been suggested as indications of various degrees of deficiency The beriberi syndrome of paralysis of the legs with atrophy of the leg muscles, edema, followed by paralysis of arm muscles, vasomotor symptoms and cardiae dilatation is well known in the orient but rare in this country

Soma Weiss and R. W. Wilkins¹⁸ report a clinical study of cases of myocardial disease in which vitamin B₁ deficiency was thought to be an important etiologic factor. They collected 120 cases in which cardiovascular dystunction of varying severity could not be ascribed to the usual etiological factors. While detailed histories frequently were not available a majority of the patients were alcoholics and many showed evidence of taulty dictary habits. In a small group with adequate data the Cowgill formula requirements were not met. In others the dietary intake was sufficient but there were associated digestive disturbances suggesting improper absorption or utilization of vitamins Suggestive evidence of beriberi and pellagra was frequent and scurvy appeared in some In others the cardiovascular symptoms were the only manifestations of deficiency

The author's tables show the suggestive symptoms

Noncirculatory

Peripheral neuritis Hypoproteinemia
Psychosis Optic neuritis
Glossitis Dysphagia
Constipation Hoarseness
Diarrhea Aphonia
Dermatitis Spooned nails
Anemia Purpura

Circulatory

Prominent cardiac Symptoms— Tachycardia with palpulsation Pulmonary rales pitation Fatigability Engorged veins Dyspnea on exertion Gallop rhythm Warm extremities Cough Edema Pistol sounds Dilated heart Orthopnea Cyanosis Paroxysmal dyspnea Signs-Syncope Circulatory collapse Tachy cardia Bronchopneumonia Embryocardia

Systolic murmurs

Diastolic murmurs

Electrocardiograms were done in 67 Ninety-three per cent showed abnormalities, the most frequent of which was a change in the direction of the Twave Sinus tachycardia and prolongation of the Q-T were also seen frequently Administration of vitamin B₁ resulted in return to normal Measurements of blood flow were of interest in that these cases did not show the slowing usually seen in cardiac failure, in fact the bounding pulse, warm extremities, flushed color all pointed to generalized arteriolar dilatation. These signs disappeared with vitamin B₁ therapy The frequency of this type of cardiovascular disorder in hospital practice was 1 160 admissions to the medical wards, but the authors point out that this obviously depends upon the social and racial status of the patients

Pathologic study of the heart muscle in cases dying with peripheral neuritis, pellagra or other evidences of deficiency show hydropic degeneration with intercellular edema and collagen. Comparison with controls showed a higher incidence of this change in the vitamin deficient group. The authors feel that the cases described by them correspond in many particulars to those reported in the orient as having "beriberi hearts," although there are many differences

A possible relationship between vitamin B deficiency and achlorhydria has been pointed out by P M Joffe, and N Tolliffe. 19 Gastric analyses on alcohol addicts revealed an incidence of achlorhydria of 33 per cent as compared with the normal expectancy of 11 per cent reported by Bloomfield and Polland The cases were analysed in an effort to determine whether the greater incidence of deficient secretion was due to alcohol per se, to vitamin deficiency (which usually accompanies alcoholism, in the authors experience) or to an associated macrocytic anemia and liver disease. It was found that achlorhydria was not related to the degree of duration of alcohol addiction, and that it did not occur with greater frequency in those with macrocytic anemia or evidence of liver dysfunction The authors concluded that there is an achlorhydria preventive factor in the vitamin B complex but suggested that it may not be identical with either the antineuritic or the antipellagra factors since achlorhydna is not frequent in oriental beriberi and not always associated with pellagra

Macrocytic anemia in pregnancy has been studied by K. O. Elsom and A. B. Sample ²⁰. The resemblance of this type of anemia to primary permicious anemia and other macrocytic anemias suggested a possible deficiency factor. Eleven pregnant women were examined every ten to 14 days with special attention to alterations of the tongue, gastrointestinal symptoms, paresthesias, impaired vibra-

tory sense, susceptibility to fatigue, edema and tachycardia. Electrocardiograms, orthodiagrams and gastric analyses using 50 cc of seven per cent alcohol, and careful blood studies were done frequently

By calculating the vitamin B requirements by Cowgill's formula and careful dietary check it was found that eight of the patients had an adequate diet at the beginning of pregnancy but began to have deficient intake on about the 245th day. At about this time evidences of deficiency began to be noted. Three patients were fed adequate diets as controls During the deficient period the blood counts began to show a decrease in the number of red cells, an increase in mean cell volume and mean cell hemoglobin, macrocytosis, reticulocytosis, polychromatophilia, poikilocytes, and young white cells No significant change in gastric acidity occurred From a clinical standpoint alterations of the tongue, and neurological changes occurred in all subjects, with other changes less frequent as shown in the following table

| Symptoms | No Pts | Time of Relief After Therapy (Aver) |
|---|---------------------------------|---|
| Tongue changes Paresthesias Fatigue Edema (, I Symptoms Blood changes Vibratory sense Tachycardia | 8 7 6 5 5 8 8 | 14 days 18 " 14 " 26 " 17 " 21 " 19 " |

The treatment employed consisted of 2 cc liver extract (Lilly 343) intramuscularly daily, and 21 grams of brewer's yeast (Harris) by mouth daily

A relationship between vitamin B, serum proteins and edema was noted by H Field, Jr ²¹ The occurrence of edema in patients receiving adequate proteins

by K Elsom in 1935. Field reports several patients with edema and lowered serum proteins which were relieved by vitamin B therapy. In some of these the edema disappeared on vitamin therapy before the serum protein had reached the "critical level," and in one patient with portal cirrhosis edema and lowered protein recurred three times on cessation of vitamin administration.

Treatment—The use of crystalline vitamin B_1 is discussed by M G Vorhaus 22 The primary value of this potent source is in extreme cases of beriberi, but it has proved of value in other conditions. The author reports treatment of over 250 cases of neuritis of various types with relief in about 90 per cent. This improvement was noted in cases of infectious origin as well as in alcoholic polyneuritis. Use of this form of vitamin therapy is suggested in cases of pregnancy where anemia, achlorhydria, denuneralization, polyneuritis and toxemia are suggestive of deficiency.

Because of the suggested relationship between vitamin B and carbohydrate metabolism, Vorhaus studied a group of diabetics. In the majority of true diabetics no beneficial effect was noted from B₁ therapy. A few cases, however, who showed other evidences of deficiency such as obesity, anorexia, polyneuritis and low metabolic rates responded well to B₁ therapy with improvement in their carbohydrate tolerance. Since these cases are difficult or impossible to differentiate from true diabetes, the author feels that B₁ medication in clinical diabetes is indicated.

Certain cases of subnormal metabolism without evidence of hypothyroidism and who do not respond to thyroid extract have been treated with vitamin B with clinical improvement, according to Vorhaus

The author suggests administration of from 1000 to 2000 Sherman-Case units (250 to 500 international units) of B_1 daily. This dosage must be continued for from four to 12 weeks. If response is not obtained with this dosage after three to four weeks, further administration is not beneficial, in the author's experience. A preliminary intensification of neuritic pain is not uncommon, occurring in 20 per cent of the cases in from three to five days. Large doses and prolonged therapy have produced no demonstrable ill effects

Requirements—Little information is available regarding requirements and utilization of vitamin B in humans E M Knott²³ conducted 23 balance studies on eight children from four to seven years of age It was found that higher retentions accompanied higher intake Optimal retention appeared when ingestion reached about 27 international units per kilogram of body weight, a figure six to seven times greater than the minimal requirements given by Cowgill torially the J A M A 24 suggests that this wide difference between optimal and minimal requirements may aid in explaining the reported frequent mild degrees of deficiency and the frequent benefit derived from vitamin B feeding in apparently nondeficient children

Elsom gives the minimal requirements as being about 1000 Sherman units (250 international units) but suggests that the optimum is probably four or five times this amount

Vitamin C

Identification and synthesis of the antiscorbutic vitamin was accomplished in 1932 Szent-Gyorgyri (1928) had found large amounts of a material which he called hexuronic acid in the adrenals of animals and in certain foods, especially oranges and cabbage Szent-Gyorgyi and King working independently identified

hexuronic acid with cevitamic acid or vitamin C and reported synthesis in 1932

Pathology-In experimental studies on the development of scurvy it has been found that some animals have the ability of synthesizing cevitamic acid The cow. rat, mouse, prairie dog, pigeon and domestic fowl do not require dietary vitamin C yet it appears in their livers. Guinea pigs and monkeys develop scurvy when deprived of adequate vitamin C. Wolbach (loc cit) describes the primary pathologic effect of deficiency as the failure of supporting tissues to produce and maintain intercellular substances The effect is on the mesodermal tissue in contrast to ectodermal and endodermal tissue as in vitamin A deficiency. The intercellular substances concerned are the collagen of all fibrous tissue structures, the matrices of bone, dentin and cartilage, and all nonepithelial cement substances including that of the vascular epithelium Hemorrhages in regions subjected to strain, edema and degeneration of skeletal and cardiac muscle are mani-Anemia also festations of deficiency occurs as a result of bone marrow degeneration and replacement by a homogeneous amyloid-like material Calcium metabolism is not primarily effected, the bone changes resulting from lack of elaboration of intercellular materials needed in growth and repairative processes Histologic repair occurs rapidly on administration of vitamin (

Symptoms — Deficiency, if marked, results in scurvy which is characterized by pale skin with numerous petechiae or subcutaneous hemorrhages, lesions of the gums, mucosal bleeding, soreness of the joints, emaciation, edema. With the development of clinical laboratory methods of analysis of blood and urine subclinical states of mild deficiency are being recognized, and a large amount of

literature dealing with animal experimentation has appeared. According to McCollum (loc cit.) normal adults carry from 1.0 to 23 mgm. per cent in the Children on poor diets have blood shown figures from 0 687 to 0.917 mgm. per cent Patients with mild symptoms suggesting deficiency had 0.254 to 109 mgm per cent which could be raised by diet to 431 mgm per cent Response to administration is rapid but storage is transient. The minimal requirement compatible with health is as yet not definitely known, but has been stated as being about 30 mgm daily for normal adults Some authors believe children require twice this amount. Adults excrete in the urine if the intake is greater than 40 mgm under normal conditions Various disease states are associated with increased tolerance It has been found that in active tuberculosis as much as 100 to 200 mgm may be given before urinary excretion occurs

The value of an intravenous tolerance test in determining deficiency has been shown by I S Wright, A Lilienfeld and E MacLenathen 25 Oral administration was found to give great variations due to deficient absorption and utilization For example, three patients were given 1 gm of cevitamic acid daily by mouth and reached an excretion level of 385, 503 and 207 mgm respectively 1 gm was given intravenously, however, the excretion reached 900, 1048, and 890 mgm Saturation had been reached orally but failed to be demonstrated by urmary excretion until the cevitamic acid was given intravenously Further study of intravenously administered vitamin C showed that 80 per cent of the amount excreted in 24 hours appeared during the first five hours after injection. This lead to the formulation of the following technic to permit of a more convenient clinical test

1 On the day of the test the patient omits breakfast, and after voiding is given 1 gm of cevitamic acid in 10 cc of physiologic saline intravenously

2 All urine for five hours is collected and immediately titrated for vitamin C content. The authors used a modification of Tillman's 26-dichlorophenolindophenol method.

A normal excretion is considered as 400 mgm. The possible effects of various types of renal damage have not yet been sufficiently studied, as a rule, however, excretion of less than the above amount indicates deficiency and excretion of larger amounts indicates adequate saturation.

Rôle of Vitamin C in Resistance-D. Perla, and J. Marmorston²⁶ have reviewed the literature on the importance of vitamin C in the maintenance of body resistance. The natural resistance of any cell depends upon the maintenance of normal cellular metabolism. It is known that vitamin C is closely related to the oxidation-reduction systems of the body It is similar to the adrenal cortical hormore in this respect. Studies have shown that vitamin C deficiency has little effect on the formation of natural antibodies nor is the formation of specific immune antibodies greatly interfered with severely deficient animals skin sensitivity seems to be decreased although skin reactions and anaphylactic responses may be obtained in mildly deficient animals In both animals and man it has been found that latent scurvy is associated with marked increase in susceptibility to drugs and bacterial toxins. Clinical experience has shown a decreased resistance of scorbutic patients to spontaneous infections, a finding which previously led to the belief that scurvy was an infectious disease Experimentally induced infections in animals have led to conflicting results It appears that certain bacteria are capable of synthesizing

vitamin C, for instance subacute infection with staphylococci may inhibit the occurrence of scurvy in animals on a vitamin C deficient diet However, scorbutic guinea pigs seem more susceptible to some infections, especially with the pneumococcus In guinea pigs with vitaniin C deficiency, infection with certain organisms such as the beta streptococcus induces arthropathy with endocardial and myocardial lesions resembling those of rheumatic fever in humans resistance of guinea pigs to chronic infections such as tuberculosis seems lowered by vitamin C deficiency and intestinal lesions are more common

In view of the indications that vitamin C deficiency decreases resistance to infection several investigators have tested the effects of hypervitaminosis C. It appears that a moderate excess may increase the natural resistance of guinea pigs to diphtheria toxin, tuberculin and to anaphylactic shock. An excess given parenterally raises resistance of monkeys to poliomyelitis. There is no conclusive data on the benefits of hypervitaminosis in humans, according to Perla and Marmoriston.

There is a great deal of evidence that vitamin (is important to normal dental development. The effect of deficiency is seen not only in the gums but in the pulp and peridental tissue as well

The work of Jusatz has been reviewed editorically in the J \ M A 27 The conclusions are at variance with those of Perla and Marmorston regarding the importance of vitamin C in specific antibody formation. Rabbits were fed deficient diets and tested for bactericidal power and production of specific antibodies. A reduction was found in both Various vitamins were then administered and it was found that little or no change occurred from the use of vitamins A, B, or D. With massive intravenous doses of

| TABLE 2 | | | | | | |
|---|--|--|--|--|--|--|
| ACORBIC ACID EXCRETION AND EXTENT AND ACTIVITY OF TUBERCULOUS INVOLVEMENT NUMBER OF CASES IN EACH GROUP | | | | | | |

| Daily Exerction | Non- | Minimal | | Moderately Advanced | | Far Advanced | | Total |
|---|-------------------------|------------------------|-----------------------|------------------------|--------------------------|-----------------------|------------------------|---|
| | Tuberculous | Inactive | Active | Inactive | Active | Inactive | Active | |
| 0 5 mg 5-8 mg 8-14 mg 14 or more mg Total | 0 0 0 10 10 | 0 0 7 3 10 | 0 1 1 0 2 | 10 17 10 39 | 7 12 17 1 37 | 0 1 0 2 3 | 7 5 3 0 15 | 16 29 45 26 Total Cases 116 |

(Courtesy Amer Jour of Digestive Diseases and Nutrition August, 1937)

cevitamic acid, however, changes were noted in the production of specific anti-A tenfold increase in specific antibody titre (horse serum antigen) occurred in the animals receiving cevitamic acid as compared to the control group When 100 mgm of cevitamic acid was administered with each immunizing dose of horse serum a similar rise occurred. These findings suggest possible applications of the use of cevitamic acid in specific diagnosis and vaccine therapy of chronic bacterial intections. An important role for cevitamic acid in allergic and anaphylactic phenomena is also suggested

In Tuberculosis - Experimental work with tuberculosis is summarized by G. J. Martin and F. H. Heise 28 Chronic vitamin C deficiency combined with progressive tuberculous intection causes a significant shortening of the survival period and a significant decrease in the body weight of guinea pigs, according to Greene. It has also been shown that animals with chronic tuberculosis were more easily precipitated into acute scurvy. However, it has not definitely been shown that hypervitaminosis in animal tuberculosis is of any great value, although this point is still unsettled

In humans, there is evidence that deficiency renders a patient increasingly susceptible to tuberculosis and that adequate vitamin C improves the prognosis The authors studied 150 uncomplicated pulmonary tuberculosis patients and 15 nontuberculous normal controls Urinary excretion of ascorbic acid was determined by titration of the 24-hour urine specimens All persons tested were on the regular sanıtarıum diet. Data was obtained on the extent and activity of the tuberculous process. The results were tabulated according to ascorbic acid excretion and extent of disease in 116 cases with an additional ten controls normal controls were found to excrete 14 mgm or more. The comparative results are shown in Table 1

It will be noted that, generally speaking, all cases of pulmonary tuberculosis have a hypovitaminosis C, and the degree seems to parallel roughly the extent and activity of the lesion. It is of interest that in ten cases followed over a period of five months, improvement was associated with increased ascorbic acid excretion. In two patients a sudden fall in excretion was found coincident with extension of the disease.

Classification of 113 patients as to whether the lesions were progressive,

stationary or improved produced the data that all with progressive lesions excreted less than 8 mgm of ascorbic acid, while the majority of the stationary or improved group showed excretion in excess of this amount. There was also a close corelation between the sedimentation rate and ascorbic acid excretion—the more rapid the rate, the less the excretion, as a rule

Response to vitamin C administration was also studied. For two weeks four ounces of orange juice were given daily (55.2 mgm ascorbic acid by titration) to 41 patients to determine a possible saturation point. Approximately 50 per cent became saturated Of 15 active cases only one became saturated, while of 26 mactive cases 20 became saturated From these studies the authors conclude that the daily requirement of vitamin C for tuberculous patients may safely be put at 110 mgm (about eight ounces of orange juice) Those patients not responding to this dose may be considered te have either a deficiency of absorption or a markedly increased demand for ascorbic acid. To eliminate the question of absorption intravenous mections of 200 mgm of cevitamic acid were given daily to ten of these non-responding patients Seven responded positively three did not. This indicates an abnormality in the intestinal tract causing destruction of or deficient absorption of ascorbic acid in a large percentage of those not responding to oral administration. In this study no evidence was obtained of the effect of ascorbic acid on the course of pulmonary tuberculosis, although the large majority of cases showed evidence of hypovitaminosis C which roughly paralleled the extent and activity of the disease Eight attempts to control hemorrhage in tuberculosis by intravenous injections of ascorbic acid were not successful

The authors state that there is probably a poly-deficiency in pulmonary tuberculosis, although other deficiencies are not yet easily measured. Such multiple deficiencies are not characteristic of tuberculosis, but may be seen in any chronic disease and many acute diseases with fever

In Wound Healing-Since the relationship of ascorbic acid deficiency to collagen formation has been established. T H Lanman and T H Ingalls²⁹ investigated the possible relationship between vitamin C deficiency and wound healing Guinea pigs were made moderately deficient and the healing of an operative wound studied. It was found to be inferior both histologically and physiologically in the deficient animals as compared to controls The normal wound is thought to reach the greater part of its strength in ten days but partially deficient animals had inferior tensile strength in the wounds as compared with controls in 10, 20 and 30 days. The scars in deficient animals ruptured with a pressure of about one-third that used in the normals

In Peptic Ulcer—It is generally agreed that alterations of tissue resistance are of etiologic importance in peptic ulcer Because of the relation of vitamin C to tissue resistance A Rivers and L. A. Carlson 30 have studied its presence in ulcer patients. It was found that in patients on approved ulcer diets vitamin C deficiency is common, especially in those having repeated hemorrhages This latter group was shown deficient by dietary history, blood and urine determinations and capillary fragility tests in all except one case. These authors considered 09 mg per cent in the blood and more than 15 mg in the 24-hour urine to be normal ministration of 500 mg per day in divided doses for three days followed by

200 mg per day for six weeks resulted in marked general improvement in all cases, although no statement is made as to any direct effect on the hemorrhagic tendency

In Whooping Cough - Treatment of pertussis by cevitamic acid in 27 cases is reported by M. J. Ormerod, B. M Unkaug, and F D White 31 Divided doses of cevitamic acid were given daily beginning with 350 mg. and gradually The latter dose reducing to 100 mg was continued until cure was effected Clinical changes occurred in the following order 1 Marked reduction or complete arrest of vomiting 2 Reduction or disappearance of night cough. 3 Reduction in number and intensity of cough spasms 4 Reduction in number and intensity of day cough spasms It was noted that as improvement occurred the daily requirement of ascorbic acid decreased

Diuretic Action—M A Abbasy ¹² reports that in children under controlled conditions ascorbic acid injections produced a marked rise in the volume of urine. The mechanism of the result is suggested as an effect on the affinity of blood for water, a dilution effect. Vitamin C has been shown to lower osmotic pressure of blood in experimental adrenal deficiency. The use of vitamin C as a mild diuretic is suggested by the author.

Daily Requirements — There is no agreement as to exact requirements. Mc-Collum (loc cit) states that the minimal requirement for normal adults is 27 to 30 mg, and that amounts more than 40 mg will be excreted in the urine M. Van Ekelen¹³ gives the figure as 60 mg for a 70 kg adult ¹⁴ C. G. King gives the figures of 25 mg for infants and 40 mg for adults per day. It has been noted above that many conditions may increase the requirements, and disturbances of absorption and utili-

zation are probably common. Most writers accept an excretion of from 14 to 20 mg as being normal Martin and Heise found an average of 14 mg per 24 hours in their controls, Youmans gives 20 mg as normal 24-hour excretion, Rivers and Carlson considered an excretion of more than 15 mg. to be normal. The latter writers used 0.9 mg, per cent as the normal blood level, while MacCollom states that normal adults may show figures of 10 to 23 mg per cent Saturation is reached at 13 mg per cent, according to Van Ekelen Using the intravenous saturation test of Wright, et al., an excretion of 400 mg or more in five hours after administration of 1 Gm is considered normal

Vitamin P

A new antihemorrhagic vitamin factor was described in 1936 by St Ruszvak and Szent-Gvorgyi and is discussed by Perla and Marmorston (loc cit) This factor, vitamin P, is intimately associated with vitamin C. In certain types of purpura associated with increased permeability and fragility of capillary walls cevitamic acid is ineffective. Such a condition readily responded to extracts of Hungarian red pepper. These extracts also decreased capillary permeability to proteins. The active principle seems to be flavouol which used intravenously in doses of 40 mg per day decreased capillary tragility and spontaneous bleeding in hemorrhagic purpura. Further investigation of this factor showed that animals on a scurvy producing diet plus vitamin P obtained from lemon juice developed scurvy as did the controls but showed less hemorrhagic tendencies 1-xperimental scurvy is apparently caused by the combined lack of vitamins C and P. Pure lack of P produces no clinical symptoms but does modify the pathologic

condition in vitamin C deficiency, according to St Ruszyak and Szent-Gyorgyi

According to Wolbach (loc cit), the physiologic rôle of vitamin D (the antirachitic vitamin) in the metabolic processes concerned in the deposition of calcium phosphate in bone is not yet clear In experimental animals, proper amounts and ratios of calcium and phosphorus prevent rickets even in the absence of vitamin D, yet vitamin D also cures tickets. The pathology of rickets arises from retardation and suppression of sequences primarily concerned in the formation of bone from cartilage and the calcification of bone matrix. This is manifested by an increase in the width of the epiphyseal cartilage and an irregular border on the diaphy-seal side in states of deficiency Later, disappearance of the cancellous bone of the diaphysis, resorption of cortical bone and deposition of subperiosteal osteoid occurs, associated with the well known deformities of nikets

The chemical nature of vitamin D in fish oils has not been definitely determined but it is known to be closely related to calciferol, which is crystalline vitamin D prepared from ergosterol by F Bills 55 states that rradiation C vitanim D occurs rarely in food stuffs but is formed in the skin by action of ultraviolet light. It develops in some food stuffs by madiation. From irradiated cigosterol it can be isolated and crystallized. The pure substance in irradiated eigosteiol (viosterol, etc.) is calciferol Several forms of vitaniin D have been tound or synthesized with slight variations in their chemical composition Ergosterol, cholesterol and sitosterol each give slightly different results to irradiation, and the resulting vitamin D may vary in its activity from that found in cod-liver oil. Eight forms had been produced at the time of writing and

there are numerous additional possibili-

Dosage—McCollum (loc cit) gives therapeutic dose as 1000 to 1500 international units per day while the prophylactic dose is about 400 international units The problem of vitamin D intoxication has been studied by I E Steck, H Deutsch, C I Reed, and H C Struck 36 There have been reports of the benefits of massive doses of this vitamin in such conditions as tetany, allergy, hay fever, arthritis, etc. Some warnings have also appeared as to possible overdosage In experimental animals (dogs) it was found that with doses greater than 50,000 units per kilogram of body weight per day the average survival period was 12 days, with amounts between 20,000 and 50,000, 39 days, and with 20,000 units or less, 68 days Chemical and microscopical examinations were conducted on tissues removed at death Previous work showed that the kidney was the most vulnerable organ to the calcifying effect of vitamin D In normal dogs the calcium content of kidnevs ranges from 29 to 301 mg per 100 (im of dried tissue with a mean of 85 The kidneys of the above animals showed that with the largest doses the average calcium content was 564 mg per 100 (m) of dired tissue, the middle group 921 mg, and with the smaller dosage, 183 mg. The lower figures in the first group may be explained by the shorter survival period. Little correlation between plasma calcium and kidney deposition was found

Microscopic changes varied in degree from degeneration of individual cells to masses of degenerated cells with calcium deposition. In general, the tissues showing the highest chemical levels of calcium also showed the greatest amount of cellular destruction. The first changes were in the collecting tubules. In other tissues the changes were variable. It is of interest that in only four of 64 dogs examined was there any medial thickening in arteries. All dogs showed absorption of fat deposits and weight loss. From these experiments the authors concluded that, in dogs, doses up to 20,000 units per kilogram per day for periods up to 153 days were not seriously injurious. It was also found that in dogs made toxic and then allowed to recover there was little residual evidence of the intoxication and the kidney content of calcium was within normal range.

Although doses comparable to those used in dogs have seldom been given to humans, the authors studied a series of 773 subjects who received more than 100,000 units daily, ranging from 1500 to 35.000 units per kilogram per dav Only eight per cent showed toxic symptoms (Symptoms have been described by C I Reed,37 and consist of frequency of urmation, anorexia, persistent nausea, vomiting, diarrhea, weight loss, muscular weakness, lassitude, dull aching in muscles, dizziness disturbed muscular co-ordination and disturbed equilibrium) The evidences of intoxication disappeared promptly on stopping vitamin D administration. Any renal disturbance is considered a contraindication to the administration of large doses, and arteriosclerosis should probably also be soconsidered according to the authors There is some evidence that hypothyroidism may accentuate the pathologic effects of vitamin D

From the information at hand it appears that massive doses of vitamin D do not do irreparable damage if signs of toxicity are watched for and administration discontinued on their appearance

Vitamin D Milk—The Council on Foods of the A M A 18 believes that a moderate amount of vitamin D in addition to that which is normally obtained

is a factor of safety in nutrition and health, at least during the period of growth Because a considerable portion of the population does not consult a physician except for illness, the Council accepts the fortification of food with vitanin D Of all the common foods available, milk is most suitable as a carrier of added vitamin D. There are three methods of imparting the properties of vitamin D to milk irradiation of milk, feeding of vitamin D to cows, and addition of either natural or synthetic vitamin D concentrates Irradiated milk, containing 135 units to the quart, has been accepted by the Council Preparations of milk containing 400 units from added cod-liver oil concentrates and from ergosterol have also been accepted From experimental work it appears that irradiated milk containing 135 units per quart usually will prevent rickets in normal full-term infants in the amounts generally prescribed This amount is probably close to the minimal requirement and it is very likely that additional vitanım D may be advisable

Vitamin E

This vitamin, obtained from wheat germ oil, has been called the antisterility vitamin because of experimental work in animals. It has the ability of preventing fetal death in rats. In humans there is some evidence that habitual abortion may be prevented. (Vogt-Moller, 1932, reported normal births in 17 of 23 women who were previously habitual aborters, and other reports have since appeared.)

Rowntree and his associates, ¹⁹ and (1 M Dorrance and F F Ciccone, ⁴⁰ have observed that rats fed unrefined wheat germ oil developed abdominal tumors in 100 per cent of the animals so treated. These tumors were spindle-cell sarcomas, and could be transplanted.

through as many as 15 successive rats. The omentum, mesentery, small and large intestine, uterus and subperitoneal area were the sites of tumor growth. Negative results were obtained with refined wheat germ oil.

Vitamin K

While as vet vitamin K has not been proved of importance to humans its relation to hemorrhagic conditions in fowls is of interest H Dani, F Schonheyder, and L Lewis⁴¹ found that deficiency resulted in bleeding phenomena in chicks, ducklings, geese Pigeons and canaries were only mildly affected while mammals (dogs rats, guinea pigs) are apparently not affected at all Vitamin K can be prepared from alfalfa and seems to have some relation to the formation of prothrombin. The authors suggest that the reason that some animals do not show evidence of deficiency is that they are either able to synthesize this vitamin or that it is synthesized by bacterial action in the intestine

Fat Soluble T Factor

An accessary food factor having an effect on the number of thrombocytes (platelets) in the blood has been described by F Schiff and C Hirschberger 12 In 1932 Schiff gave a diet rich in lipoids to patients with lipoid nephrosis and found a striking rise in thrombocytes. A similar rise occurred in a case of thrombocytopenic purpura Fgg volk and vitamin A in oil were effective as was carotene in oil vitamins C and B were not It was discovered that the stimulating effect was not due to the presence of vitamin A but to something in the sesame oil used as a solvent A normal hild given eight to ten drops of sesame oil daily developed a rapid and marked rise in platelets Cod-liver oil and olive oil produced no effect. The possible clinical value of this discovery has yet to be investigated

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DISEASES OF THE RESPIRATORY TRACT

By FRANK WALTON BURGE, M D

In the last two years, much has been seen in the literature attesting to the open-mindedness of clinical investigators working in the pulmonary disease field

Asbestosis does not develop until from 5 to 15 years after the beginning of inhalation of asbestos dust, according to the investigation of L. Martz. There is no increased tendency to tuberculosis in the asbestosis case according to the investigation of A. J. Lanza and his associates.

Much has been done in advancing earlier diagnosis of pulmonary careinoma. R. Overhold justifies exploratory thoracotomy following diagnostic pneumothorax, when careinoma of the lung is suspected without loss of time and presents the importance of bronchoscopic study of such cases.

Pleuropulmonary complications of ameliasis occur in over 15 per cent of cases. The clinical signs are cough, expectoration, fever, diarrhea, enlarged and tender liver, pain in the chest, and cachexia. Expectoration of chocolate-sauce pus is of diagnostic importance. Ame-

bas may be found in the sputum. The treatment is emetine, aspiration of the abscess, and, if complicated with secondary infection, open drainage, according to A. Ochsner and M. DeBakey.

Pneumonokoniosis

Incidence of Tuberculosis in Silicotics—A S Pope1 reports that examination of 961 quarrymen in the same towns in Massachusetts showed that 219. or 22.8 per cent, showed roentgenologic signs of silicosis. With the reasonable assumption that the tuberculosis mortality, unconnected with silicosis, among these stone cutters is essentially the same as that for males of corresponding age in the community, there still is an excess of eight tuberculosis deaths a year in that group, which may fairly be charged to less than a tourth of the 793 cutters, or roughly to 180, equivalent to an annual mortality rate of 4400 per hundred thousand approximately 40 times the expected tuberculosis mortality

Since the original examination during the summer of 1933, it has been found

possible to check the roentgenologic diagnosis of silicosis and tuberculosis in a certain number of quarrymen in one city Five with that classification have developed positive sputum, and three others who have come to necropsy all showed definite macroscopic and microscopic evidence of coexisting silicosis and tuberculosis The fact that the diagnosis of silicosis or of silicosis with tuberculosis is often made on insufficient evidence or by mexperienced physicians, in no way detracts from the importance of silicosis as an industrial disease or from the demonstrated frequency or seriousness of tuberculosis as a complication of silicosis

Bronchomycosis

R Fawcitt finds that this disease of haymakers and harvesters, is a fungus disease of the lung which is readily curable by potassium folded therapy

Treatment of Bronchopneumonia

Treatment of bronchopneumonia in infants by ctrated blood transfusions following bleeding is advocated by P Rohmer and B Tassovatz

Empyema

Treatment II koster and his associates claim children should be treated by drainage, followed in two or three days by artificial pneumothorax to the contralateral side, as the procedure tapidly expels pus from the infected side, reexpands the lung on the infected side thus hastening recovery the patients becoming afebrile in one week and the pus drainage stopping in less than two weeks. The above method is applicable to adults, also

Postoperative Pulmonary Complications

A H Miller² believes that the choice of method and care in the administration

of anesthetics are important factors in the prevention of postoperative pulmonary complications

Balanced anesthesia is the first consideration. This in combination with the regional use of procaine, provides muscular relaxation and permits surgical manipulation under a lighter general anesthesia.

An excess of oxygen, with entire absence of anoxemia is important, as is the aseptic maintenance of the anesthetic apparatus, which prevents the carrying of respiratory infection from one patient to another. An even depth of general anesthesia should be maintained and the deeper zones avoided. Careful attention should be given to minute details having to do with the care of the patient in the operating room and during the period of recovery.

Pulmonary Abscess

Pathology — Modifications of Peripheral Blood in Pulmonary Abscess — A Bertola and M Ravetta's studied the modifications of the peripheral leukocytic formula and of the myelogiam in eight cases of pulmonary abscess. In five cases the abscess was of metapheumonic origin, in two cases it developed in patients suffering from chronic bronchitis, and in one it was an amebic abscess of the lung.

The blood for counting cells was taken from fasting patients. The puncture for obtention of the sternal medulla was done at the second and third intercostal space with a needle long enough to obtain fragments of medullary tissue. The myelograms were made by examination of several slides, with no less than 1000 or 1500 cells on each slide.

In cases which follow a grave evolution there is a relative increase of the granuloblasts in the blood and in the medullar tissue and absence of eosinophils in the blood and of myeloid and histoid cells with eosinophil granulations and of plasma cells in the bone marrow In cases which follow a favorable evolution there is a relative increase of ervthroblasts in the bone marrow and diminution of the leukoblasts also eosinophilia and increase in the bone marrow of myeloid and histoid cells with eosmophil granules in different stages of maturation and increase of plasma The formation of erythroblastic cells tissue in the bone marrow is of good prognosis and there is a relation between the modifications of the blood and of the hematopoietic organs in the course of pulmonary abscess and the etiology and evolutional phase of the condition

The Anatomicoclinical Forms and Diagnosis of Pulmonary Abscess—E Sergent, H Durand and R Kourilsky⁴ state that there seems to be no doubt that suppurations and primary cancer of the lung are much more frequent than formerly, and that the increase is real and not due merely to improved methods of diagnosis

These suppurations are classified into diffuse and circumscribed The diffuse forms may be acute or chronic. Among the acute forms are dissecting pneumoma, diffuse suppurated bronchopneumonia, and multiple abscesses from pyo-The chronic forms are septicenna manifestations of purulent bronchorihea and particularly of dilatation of the bronchi Circumscribed suppurations include two distinct groups supputations in pre-existing cavities and abscesses properly speaking. The secondary suppurations in pre-existing cavities include intrapulmonary congenital cysts, juxtapulmonary dermoid cysts, hydatid cysts, and hematic cysts Abscesses properly speaking generally result from acute They may result from ınflammation

the necrosis of a cancer or a syphilitic gumma

Abscesses may be divided into the simple and the complicated. Simple abscesses include amebic abscesses, abscesses from pyogenic cocci, and abscesses which are putrid from the beginning. Complicated abscesses include simple abscesses which have passed into a chronic condition and abscesses associated with other affections such as bronchiectasis, pleural effusion, and tuberculosis

Treatment—C L Harrell says lung abscess should be treated early with *pneumothorax*, but the amount of collapse should be much less than in tuberculosis treatment, just enough gas being kept in the pleural space to expedite drainage. He reports excellent results with this treatment, 52 per cent complete recovery.

The Anatomicoclinical Forms and Diagnosis of Pulmonary Abscesses—E Sergent, H Durand and R Kourilsky (loc cit) state that recovery results in 70 per cent of cases of pyogenic abscesses and 30 per cent of those of putrid abscesses. This fact renders the interpretation of different medical treatments doubtful. Some of them are only apparently successful as recovery would have occurred spontaneously.

Before operation is considered, the patient should be given a chance to recover spontaneously. No matter what organism is responsible for it, the abscess generally resolves in from six weeks to two months if it is going to resolve spontaneously. Therefore if cure has not taken place spontaneously or under medical treatment at the end of two months, operation should be performed, otherwise, the abscess will be more difficult and less likely to be successful

The only reliable evidence of cure is total clinical and roentgen repair of the lung parenchyma, no matter whether

the abscess is one of the pyogenic or the putrid type. If this fact is borne in mind, the physician will not be deceived by false cures. If the outline of a cavity disappears and is replaced by an opaque zone, operation should be performed if two months have elapsed since the beginning of the infection.

There is a radical difference between pyogenic abscesses and putrid abscesses. The latter are much more serious on account of their tendency to indefinite recuirence. This is due to the persistence of bacteria, probably spirochetes, in the walls of the abscess. Therefore, simple pneumotomy is not sufficient for cure, excision even of the walls of the abscess to a certain depth is necessary. The greater the delay, the more extensive the removal necessary and the more dangerous it will be because the sclerosis keeps the bronchi and vessels fixed and gaping

The choice of operative method—pneumotomy, pneumectomy, or lobectomy—will depend upon the anatomical type, extent—site, and complications of the abserss

Benzotherapy in Pulmonary Suppurations and Gangrenes—I. Gold-korn⁵ in a previous article reported some results from intravenous injections of sodium benzoate in pulmonary abscesses. I wo time or 10 cc of a 20 per cent solution were injected from five to ten times obtaining dramage and a benign influence in expectoration. In more abundant cases it was necessary to increase the dose to 3 or 4 Gm, and from 4 to 8 Gm were injected twice daily when the condition was alarming

Of 22 cases of pulmonary abscess there were five of a septic form with rapid destruction of tissue, 15 had a duration of more than six weeks, and two were fatal. A permanent cure was obtained in 18 patients who were under observation

for three years In six cases of gangrene, the therapeutic effect was remarkable in from five to six days. The antiputrid action of sodium benzoate in doses of from 2 to 4 drams (8 to 16 Gm) made the unpleasant breath disappear completely. In four recent cases the cure was permanent. One case of six months' duration was much improved and one was fatal

In 30 per cent of the patients there were dizziness and flashes before the eyes, which lasted but a minute. For this reason it is good to proceed slowly with the injection. In three cases of pulmonary abscess there was pain in the abdomen, which lasted four minutes after the injection. A few drops of tincture of opium or belladonna relieved the symptoms. Small doses of sodium benzoate were also given in bronchopneumonias. There were no contraindications

Roentgen Therapy—P Adamowicz and Z Kulig⁶ report results with the use of roentgen rays in 11 patients who suffered from abscess and necrosis of the lungs

Complete recovery occurred in eight cases, two patients died during treatment, although at first they showed signs of improvement, and one patient relapsed after having been apparently on the road to recovery for ten weeks

It is remarkable that each patient treated with roentgen rays became worse after the first and sometimes after the second application. The patients felt weak and exhausted and their temperature rose, although their cough diminished and became milder. However, after the third application a marked improvement could be noticed.

The roentgen dosage and the intervals between treatments cannot be schematized but must be regulated according to individual cases

Pulmonary Suppuration

W E Burnett⁷ states that cough, moderate to profuse expectoration with foul odor, and a variety of abnormal chest signs indicate one of the multiple forms or combinations of pulmonary suppuration, which are fairly common

Diagnosis is made easily by using bronchoscopy, x-ray, lipiodol bronchography, judicious aspiration or even thoracic exploration

Bronchiectasis may develop from empyema, lung abscess, or spontaneously. It is a progressive lesion with an average life expectancy of from three to seven years of incapacitated living, followed by death from suppurative pneumonitis, brain abscess, or myocardial or nephritic degeneration. Lobectomy, although attended with a moderately high mortality (15 per cent), is the only successful form of therapy, and comparatively, the mortality is low.

Lung abscess may occur spontaneously, following respiratory infections, after a period of unconsciousness produced by cerebral trauma, anesthesia, drunkenness, drugs, etc., from foreign bodies, bronchial neoplasm, or lodgement of an infected embolus. One-third of such abscesses proceed to spontaneous cure \n additional 20 to 25 per cent can be cured by bronchoscopy and surgery. The remaining 40 to 45 per cent mortality is comparable to the deaths from cancer. This excessive mortality can be reduced by earlier diagnosis by those who see the patients first and by immediate proper treatment

BRONCHUS

Carcinoma of the Bronchus

L H Clerf's declares that if there is to be any advance in the surgical treatment of bronchial carcinoma, it will depend

almost entirely on arriving at a correct diagnosis early in the disease responsibility rests primarily with the clinician, who should be "cancer of the bronchus minded" as well as "roentgenray minded" When cancer is a diagnostic possibility, it is important to arrive promptly at a diagnosis. No group of symptoms or signs can be considered diagnostic of carcinoma, they are dependent on the location of the growth and its influence on adjacent structures The early symptoms are important, as their correct interpretation will lead to early diagnosis. A diagnosis made when the carcinoma is advanced is of statistical value only, from the patient's standpoint it is of little or no importance

Cough with or without sputum has been the most common early symptom of carcinoma involving the larger bronchi If associated with blood-streaked mucoid sputum in the absence of tuberculosis, it is highly suggestive of bronchial neoplasm A wheeze in conjunction with cough and occasional blood-streaked sputum or absence of sputum constitutes strong evidence that new growth is producing early partial obstruction to a bronchus Pam is not a common early manifestation of carcinoma originating in the larger bronchi. It is, however, considered 'the most common signal symptom" of peripheral carcinoma and is due to peripheral extension of the growth to the pleura and extrapleural structures

Dyspnea, pleural effusion, loss of weight, weakness, fever and sweats, dysphagia, hoarseness, pupillary changes and engorgement of the veins of the neck and chest are commonly evidences of advanced disease and are principally of didactic interest

Difficulty in diagnosis is encountered in cases in which the changes are suggestive of tuberculosis, pneumonitis,

bronchicetasis or pulmonary abscess without roentgenographic evidences of tumor Since more or bronchial obstruction than 50 per cent of primary bronchial neoplasms originate in the larger bronchi, it is evident that in many cases during the early stages there is partial obstruction to a bronchus, with obstructive emphysema Roentgenoscopic examination of the chest and a study of the roentgenograms made at the end of full inspiration and expiration aid greatly in the recognition of nonopaque foreign bodies in the bronchus and a knowledge of the mechanism of obstructive emphysema

Bronchoscopy is the most definite and positive diagnostic procedure available. One may obtain a direct endoscopic view of the growth. In addition, tissue may be secured for histologic examination. It no intrusion of growth into the bronchus can be visualized, one may observe evidences of infiltration of the bronchoscopist should be given an opportunity to investigate endoscopically all cases of obstructive emphysema or obstructive atelectasis. Unexplained cough, hemoptysis, and wheeze also warrant bronchoscopy.

Pseudo-Esophageal Form of Bronchial Cancer Rebattu Gravier and Sprecher" report the case of a male, aged 53 who asked medical advice on account of vocal disturbances which had begun suddenly during complete health, several weeks before

Examination revealed paralysis of the left recurrent nerve with immobilization of the vocal cord on the median line. The other vocal cord was practically normal, as were the other portions of the larynx. Auscultation, palpation of the neck and examination of the nervous system revealed nothing abnormal and it appeared as if the recurrent paralysis.

originated from a mediastinal lesion Later the patient developed progressive dysphagia

Repeated esophagoscopies finally suggested a submucous neoplasm of the esophagus. There were no signs of syphilis or tuberculosis. Several times the patient had blood in the sputum and bronchoscopy was resorted to. This and biopsy finally disclosed the bronchial tumor, but until the end the symptoms were those of an esophageal stenosis.

Tracheobronchial cancer is not the only lesion which manifests itself by dysphagia and stimulates esophagial cancer. All disorders in the region of the mediastinum are likely to compress the esophagus. In all mediastinal syndromes, in which the clinical diagnosis is often extremely difficult, endoscopy (esophagial and bronchial) is of primary importance and is superior to roentgenologic examinations, which do not always give conclusive results

Carcinoma of the Bronchus in Association with Anthracosilicosis—R Chair¹⁰ states that clinical and pathologic observations on four cases of primary carcinoma of the bronchus associated with anthracosilicosis disclosed the following

Dyspica, hemoptysis, cough, expectoration and pain in the chest are outstanding symptoms. Sputum negative tor tubercle bacilli (with hemoptysis a trequent symptom) excite a suspicion of primary malignant growth of the bronchus.

Roentgen-ray diagnosis of diffuse bronchogenic carcinomatosis is difficult when anthracosilicosis coexists

Extensive destruction of the bronchial cartilages, resulting in collapse of the involved bronchi, may be responsible for severity of dyspnea

Capability of the peribronchial and perivascular lymphatics to dilate in spite of fibrosis surrounding them

Spread of tumor cells through the alveolar pores and interlobar adhesions

Absence of toxic symptoms of pulmonary suppuration is attributed to impaired lymphatic absorption and lessened blood flow through the atelectatic lungs

It is possible that anthracosilicosis might have an indirect influence on development of carcinoma of the bronchus

Primary Carcinoma—L F Frissell and L C Knox¹¹ state that the physical signs of bronchial carcinoma are protean. There may be a complete absence of signs in the early stages, giving way to localized bronchitis and x-ray evidence of slight peribronchial infiltration in a few months. Later there may be dulness, bronchial voice, bronchial or diminished breath sounds, and displacement of the mediastinum and diaphragm. Abscess formation or pleurist with effusion may mask the physical signs.

The two most helpful adjuvants are roentgenography and bronchoscopy. The lesion is often situated near the opening of one of the main stem bronchi and is accessible to inspection and often to removal of a piece of the tumor for pathological examination.

Thoracoscopy may be of value in establishing a diagnosis and also in determining the possibility of a successful operation

Bronchiectasis

Treatment—The Use of Roentgen Therapy—M Berck and W Harris¹² believe that the successful use of roentgen irradiation in large dosage as the sole treatment of chronic secreting bronchicetasis has not been previously reported Favorable results were obtained in 30 cases. The rationale of the method, which is largely empirical, is based mainly upon the known effects of roentgen rays on chronic inflammatory processes. Correct diagnosis of both the site and the extent of the involvement is a

prime requisite in the treatment. The irradiation is indicated only in "wet" cases since its chief aim is to arrest the expectoration. It is considered suitable only for patients who are ambulatory and afebrile and present a chronic lesion with a more or less constant level of expectoration and without marked remissions.

Of the 30 cases treated, 14 belonged to a group secondary to chronic anaerobic lung abscess. Three were characterized by the expectoration of a moderate amount of odorless sputum, and 13 by the expectoration of large quantities of foul sputum.

Roentgen therapy in large dosage was given to these patients over a period of approximately three months All of the diseased and secreting lobes (as revealed by thorough bronchography and bronchoscopy) were cross-fired through anterior, lateral, and posterior fields From three to seven fields were irradiated The average total dose was approximately 1200 roentgens through each of the anterior, lateral, and posterior fields The physical factors of the technic were from 180 to 200 ky, a focus-skin distance of 50 cm, a current volume of 4 ma, filtration with 0.5 mm of copper and 1 mm of aluminum, and fields measuring 10 by 15 cm. Each treatment consisted of 75 roentgens, measured in air to two or three fields The treatments were usually given two or three times a week

During the course of the treatment the symptoms were usually exacerbated at first. Noticeable improvement began after approximately three-fourths of the series of irradiations had been completed. It was signalized by a gradual and progressive decrease in the cough and foul expectoration. The improvement continued for a period of at least four months after termination of the treatment. In a number of the cases clubbing

of the digits has surprisingly subsided, and in some, posttherapy bronchography showed favorable alterations in the picture of the dilated bronchial tree

The following conclusions are drawn

- 1 In chronic secreting bronchiectasis toentgen therapy in moderately large dosage as the sole method of treatment is feasible and successful, resulting in great symptomatic improvement in a considerable percentage of cases
- 2 In many cases of chronic bronchiectasis treated with moderately high dosage of roentgen therapy the improvement is so great as to approach practically complete cessation of the symptoms of expectoration and cough
- 3 Follow-up examination over a period of two years in cases in which there has been improvement has shown no recurrence of symptoms with infections of the upper respiratory tract

Results of 15 Consecutive One-Stage Lobectomies—E. J. O'Brien 13 reports 15 cases of bronchiectasis in which a Brunn-Shenstone one-stage lobectomy was performed. The one death in the series was due to pulmonary embolism and occurred on the 14th day. To re-inforce the interrupted ligatures in the end of the stump a mass ligature is placed in the groove formed by the tourniquet. Rapid re-expansion of the remaining lobe is insured by the application of constant low-pressure suction to three dramage tubes.

Lobectomy and Pneumonectomy 1n Bronchiectasis and Cystic Disease—

E D Churchill¹⁴ recorded a mortality of 6 l per cent in the cases of 49 patients upon whom lobectomy or total pneumonectomy was undertaken for bronchiectasis or cystic disease, and a mortality of five per cent was recorded for 40 patients upon whom lobectomy alone was done. In the cases of 38 patients subjected to lobectomy by methods now

recommended, the mortality was 26 per cent. The last 30 successive lobectomies, including one with the removal of the right middle lobe as well as of the left lower lobe, were completed without mortality

Two surgical programs are available one-stage lobectomy, and two-stage lobectomy Each proceure has its indications. A choice should be made according to the problems presented by the individual patient. The total number of postoperative days in the hospital are approximately the same following the two operations.

If a two-stage lobectomy is chosen, it is strongly recommended that the second stage of the operation should not follow the first too closely. Symptomatic and physical improvement follow the first stage of the operation in the majority of the cases, and if some time elapses the patient approaches the more hazardous procedure in an improved condition

Paralysis of the phrenic nerve as an independent procedure appeared to have little or no effect in 20 cases of basal bronchiectasis

Most lobectomies are considered elective operations and are not performed during the winter and early spring. It is believed that the exacerbation of the disease and the thigh incidence of respiratory infections during this period might increase the risk of operation.

LUNGS

Primary Carcinoma of the Lung

L F Fitsell and L C Knox¹⁵ report that primary carcinoma of the lung is not the rare disease that it formerly was believed to be, but the question as to whether the increase is real or apparent is still open to debate. It must be taken into account that many tumors classified as carcinomas by pathologists of the

previous century are now called epithelial tumors of the so-called oat-cell variety, and carcinoma of the lung formerly was usually considered metastatic. Also, wide-spread interest has led to the discovery of a considerable number of small pulmonary neoplasms with large metastases, such as were undoubtedly regarded by earlier observers as the primary lesions. It is believed that the increase in incidence of bronchial carcinoma in the past two decades is apparent rather than actual

Etiologically, carcinoma of the lung must be dependent in general on the same causes as carcinoma elsewhere

The onset of pulmonary carcinoma may be exceedingly insidious. Of 46 patients, in ten cases only could a history of over one year be elicited, though in two others asthma had been present for many years.

Carcinoma of the lung is almost entirely a disease of middle and later life. By far the largest number of cases occur between the ages of 50 and 70 years. The ages in this series ranged from 17 to 69 years.

Primary tumors of the lung are more frequent on the right side than on the left. In this series 17 per cent involved the main bronchus four per cent were peripheral, two per cent bilateral, 32 per cent were located in the right upper lobe, 13 per cent in the left upper lobe, 11 per cent in the right lower lobe, and 15 per cent in the left lower lobe.

The classification based upon an anatomical or descriptive basis includes five types (1) The central or hilus type, 497 per cent. (2) the nodular parenchymatous type, 178 per cent. (3) the peripheral type, 65 per cent. (4) the diffuse type, 239 per cent, and (5) the bilateral miliary type, 21 per cent

Carcinoma of the lung is one of the tumors which metastasizes most widely,

involving organs not frequently affected by tumors arising elsewhere, as, for example, the suprarenal glands and the brain. In this series of 46 cases, all except one (97.4 per cent) showed metastases, at least to the regional lymph nodes

It is now almost universally accepted that the cells of pulmonary carcinoma are derived from the mucous membranes of The lining the bronchi or bronchioles of the bronchi consists of a columnar ciliated epithelium with goblet cells in between the epithelial cells, thus forming the pseudostratified respiratory epithe-Mucous and mucoserous glands are found in all portions of the bronchial tree containing cartilage. This affords three adult modifications of lining epithelium from which cuboidal, mucusproducing, or papillary adenocarcinoma may arise

The number of groups of pulmonary carcinoma which may be recognized histologically varies according to different writers. A simple classification is as follows. (1) Squamous. (2) adenocarcinoma, and (3) undifferentiated, of two sub-types. (a) carcinoma simplex including the polymorphous types of large giant cells, medullary types with small oval cells, cuboidal and cylindrical cells without acinus formation, and basal cells, and (b) small spindle-cell, or so-called out-cell, and round-cell types.

The squamous type of cell was found in 304 per cent of cases. The morphology varies. In some keratimization with extensive softening and necrosis is prominent, and there may be well developed intercellular bridges, or the malpighian layer may predominate. More frequently the differentiation is less complete and only small imperfect pearls and groups of pavement cells with early keratimization indicate the metaplasia which is in progress. Transitional cells may alter-

nate with any of these forms Among the 14 cases of squamous tumor, metastases were found in the bronchial nodes in all cases in which autopsy was performed, in the cervical nodes in two, and in the pleura, ribs, ilium, spine, axillary nodes, liver, and adrenal glands An extensive local spread may take place with infiltration of the pericardium and pulmonary vein, and constriction of the superior vena cava, and the pulmonary artery Squamous tumors may arise in any portion of the lung, and the morphology has nothing to do with the level of origin, that is, squamous, columnar, or undifferentiated tumors are not found exclusively in any one location

The adenocaremomas, constituting 26 per cent of this series, include those tumors which show definite palisading around a central glandular lumen, a tendency to replace the liming cells of the pulmonary alveoli, or to form throughout low columnar cells, usually with the production of considerable amounts of micus. Small areas of one portion of the tumor may appear definitely cuboidal, while in some other portion of the primary growth or metastatic deposits the cells may be much more detached and no true glands may be detected.

Of special interest is the bilateral miliary tumor. The cells of this tumor were unusually tall columnar cells, secreting fairly large amounts of micus. In this type of tumor, single lobules appear to be distended and filled with glarry grayish, micus-producing, cells, distributed throughout both lungs.

The adenocarcinomas are among the most rapidly growing and widely metastasizing of the lung tumors. Through their rapid extension by direct implantation and by the lymphatics, whole lobes, or even a whole lung, may become involved, and as it consolidates it closely resembles a gray hepatization of lobar

pneumonia, thus forming the so-called pneumonic form of carcinoma

The undifferentiated types of lung carcinomas comprise 41 per cent, the largest group, in this series of cases

Diagnosis—The symptoms of bronchial carcinoma are protean in character, depending upon the stage of the disease Tumors located in the primary bronchicause cough and often hemoptysis, those located centrally in the lung tissue may give no symptoms whatever. The first symptom may be due to metastases elsewhere in the body. The two most constant symptoms are cough and pain. There may be expectoration, at first of glairy, then mucopurulent, and finally purulent mucus.

With abscess formation, the sputum is foul and fetid At first pain may be merely a vague sense of boring or oppression, but later it may be more intense, and sometimes excruciating, especially when it assumes a pleuritic character Asthmatic breathing or dyspnea can occasionally be the first symptom may be caused by either replacement of a large part of the alveolar cavity by tumor tissue, or by tumor of miliary distribution, or more commonly by pleural effusion, atelectasis, or pressure by mediastmal lymph-node metastases on the trachea, bronchi, or heart Loss of weight and strength is occasionally the first sign noticed Osteoarthropathy was the first sign in three cases. Fever occurred in more than half of the patients Hemoptysis is often an early finding and often recurs

Treatment—Until recently, the outlook for patients with carcinoma of the lung was hopeless, but since the introduction of the *bronchoscope* a number of cases have been reported in which the growth has been removed without recurrence

Lobectomy and pneumonectomy have been performed successfully. Two such operations were done in this series of 46 cases

Radiation with x-rays and radium has been disappointing

The outlook for these patients is still extremely bad and less conservatism and more operation is advised, both for diagnosis and radical extirpation

Pulmonary Tumors

Irregularities of Pulse—A W. C G Kamerling and C L C van Nieuwenhuizen¹⁶ found eight patients with irregularities of the pulse among 36 patients with pulmonary tumors. Auricular fibrillation was observed in six, paroxysmal sinus tachycardia in one, and paroxysmal ventricular tachycardia in another.

Since these irregularities sometimes occur as the first symptom of bronchial carcinoma, they are of a diagnostic and prognostic importance. Vasal and sympathetic irritation is regarded as the cause of the symptom in patients with pulmonary tumors. Distinct signs of sympathetic stimulation (exophthalmos and dilated pupils) were found in some cases and necropsy disclosed a damaged vagus nerve in a few instances.

Disturbances in Cardiac Rhythm—P Formijne and P J Zuidema¹⁷ report nine patients with pulmonary cardinoma in whom cardiac rhythm disturbances were observed. The arrhythmias were all of the paroxysmal type Fibrillation appears to be the most important of these disturbances of the cardiac rhythm. It was observed in four patients. In one patient, cardiac flutter was observed and in another tachysystole. In the remaining three cases, the character of the arrhythmia could not be definitely identified.

Thirty-three pulmonary tumor cases, observed during the same period as the nine pulmonary tumor cases with paroxysmal arrhythmia, were found to be without it. The paroxysmal development of the fibrillation and flutter may be regarded as characteristic for pulmonary tumors. In most of the cases, necropsy revealed that the neoplasm had invaded the pericardium or the musculature of the auricles.

Calcium Prophylaxis of Postoperative Pulmonary Embolism

E Muff¹⁸ reports that prophylactic injections of *calcium chloride* for the prevention of fatal pulmonary embolism was first introduced at Bier's clinic

The technic is the injection of 1 cc of a 0.01 per cent solution of calcium chloride intramuscularly into the thigh or the gluteal muscle. The intramuscular injection is less painful than the subcutaneous. The injections are given daily for eight successive days after operations or injuries. If signs of thrombosis or of pulmonary infarct appear, the injections are continued for two weeks.

The treatment proved effective in over 2300 surgical cases. Since the fatal embolus usually originates in a symptomless distant thrombosis, a measure which increases the adhesiveness of such thrombiappears to be valuable.

Hemopneumothorax, Spontaneous

() R Jones and C L Gilbert studied the condition and advise removal of the blood if the amount is large, with air replacement

Pulmonary Hemorrhage

Treatment — O S Kazarnovskaya and V I Mordvinkina report that hemorrhage was arrested in 96 per cent of a

blood plasma. Thirty-three of the cases had persistent profuse bleeding which had resisted treatment with calcium chloride, autohemotherapy, and horse serum. They infused 20 to 40 cc of plasma at one time. Thirty-one cases received only one transfusion, nine cases received two, and 11 cases received three treatments.

Bilateral Spontaneous Pneumothorax in Apparently Healthy Individuals

F A Hasney and F Baum¹⁹ report a case of idiopathic spontaneous bilateral pneumothorax in an otherwise healthy young person. There was not the slightest evidence of active pulmonary tuberculosis Parahilar annular shadows seen on the roentgenogram taken after bilateral re-expansion were due to bullae described by Schmincke. The bilateral spontaneous pneumothorax was of the alternating type. The first rupture occurred on the right side and the second on the left before the right lung had had the opportunity to re-expand completely During the third attack, the left side collapsed, but an adhesion between the two left pleural layers, which must have formed after the re-expansion following the second attack, prevented complete compression of the left lung. The pneumothorax on the right following the third attack must have been so small and the opening of the superficial bulla so minute that the patient did not notice any discomfort. It was detected only by accident during the last roentgen check-up

Bed test and strapping of the chest alone do not guarantee against a further accidental collapse. It is safer to continue the pneumothorax, first on the right, artificially for a while until the x-ray observations show a thickened visceral pleura which, after re-expansion will remain adherent to the parietal layer. The

irritation by artificially insufflated air alone is sufficient. Artificial pneumothorax should be applied on the left if another accident happens. The use of irritating substances other than filtered air intrapleurally is not recommended. The ideal procedure in pneumothorax is to keep the pleural sac dry

The Editor treated a 19-year-old male in May, 1937, who had had six attacks of spontaneous pneumothorax on alternating sides in the preceding three years

Mantoux and re-Mantoux were negative, as was the lung x-ray. The last attack was on the left side. The collapse was maintained by artificial pneumothorax until September, 1937. There has been no recuirence to date.

One-Stage Pneumonectomy Under Local Anesthesia

W E Burnett ²⁰ ()f 41 reported cases of pneumonectomy, 25 were successful and 16 unsuccessful, or a mortality of 39 per cent. However, this includes the earlier cases in which the mortality was very high. In the last 30 cases reported, there were nine fatalities, or a mortality of 30 per cent.

On another case, a girl eight years of age a one-stage pneumonectomy was done under local anesthesia using a technic that has been developed from extension of the field block technic for rib resection in the treatment of empyema and partially thoracoplasty. It has been used in three lobectomies, three thoracic explorations, and on this pneumonectomy

One-half of one per cent procame hydrochloride in saline solution is used to produce a series of wheals over the intercostal spaces, from the second to the tenth or eleventh, at the edge of the erector spinae muscle. After the first injection, these are made painlessly from beneath the skin. Through these

wheals, injection of about 5 cc of one per cent procaine hydrochloride are made into the appropriate nerves. If the incision is to be carried to the midline anteriorly, the crossed innervation from the opposite side has to be interrupted by a band of procaine hydrochloride at this point. Towel clips, used in the upper pectoral region, require additional local injection into each spot.

Ten minutes after the last injection, the anesthesia is checked by the needle and finger method. If it is not complete, injections are again made into the nerves, which have not been interrupted.

When the chest is opened, inhalations of carbon dioxide and oxygen under pressure may be necessary to prevent sudden complete collapse. They are unnecessary if pneumothorax has previously been instituted or if the lung is extensively adherent. The injection made into the phrenic nerve in the thorax, when it is exposed, interrupts the sensory and motor diaphragmatic innervation.

The pulmonary ligament and the hilus of the lung are sensitive areas, and one per cent procame hydrochloride has to be injected into them. Pouring one per cent procame hydrochloride over the pleura and maintaining its application with a gauze sponge saturated with the solution while adhesions are dissected or the remainder of the thorax is explored produces insensitivity there also

Children are prepared by the preliminary injection of fairly large amounts of *morphine* in divided doses and adults by the use of ¹₆ grain (10 mg) of morphine supplemented by rectal injection of *tribromethanol*, from 40 to 60 mg per kilogram, depending on the type of person. Under these circumstances, the cough reflex is not abolished, although it is definitely decreased.

The disadvantages of this method are the same as those for most operations with local anesthesia

The advantage is that for the same procedure, the amount of shock is greatly decreased or a more extensive procedure is possible at a one-stage operation, than is possible with anesthesia by inhalation. The difficulty of certain complicated types of administration of anesthesia is avoided. The operator is able to work accurately and without haste; the cough reflex for expulsion of pus or blood as the lung is manipulated is maintained, and there is considerable improvement in immediate postoperative convalescence.

Conservation of the First Rib in Apicolytic Thoracoplasty

H Liliental²¹ secured marked local compression of the apex of the lung by combining *extrafascial packing* with a *partial thoracoplasty*.

The first rib is preserved but the lung with its overlying soft tissues is separated from it. A rubber dam is packed into the dead space and, because of its elastic spreading, the amount of compression is increased during its stay of from four to five days. Following removal of the rubber dam, the cavity is allowed to fill with granulation tissue.

This operation was used in four cases. The preservation of the first rib aids in keeping the packing in place, minimizes the danger of injury to the important vessels and nerves, and may decrease the amount of thoracoplastic scoliosis.

Modifications of Lung Parenchyma After Sympathectomy

A Brasmr²² made an x-ray and anatomic study of the modifications of the lung parenchyma in experimental cervical sympathectomy and observed that the modifications depend on the

degree of sympathectomy and the side on which it is done Unilateral sympathectomy induces reduction of the bronchioles and small blood vessels, which is more accentuated in the lung of the side on which the operation was done The modifications of the vessels and bronchioles are more accentuated after bilateral sympathectomy They are more intense at the upper field of the right The modifications induced by unilateral or bilateral sympathectomy are more accentuated a long time after the operation They are due to permanent changes in the circulation of the lung due to disturbances of the sympathetic innervation of the organ The modifications of the heart originate partially in local disorders of sympathetic innervation

Cervical sympathectomy induces elevation of the diaphragm, especially of the right side, probably through anatomic phrenic and cervicosympathetic connections. Results of experiments show the dangers of cervical sympathectomy in the clinical field and the treatment is not advised.

Complications - Postoperative Pulmonary Lesions—P Duval and I Binet23 believe that certain postoperative pulmonary lesions are caused by inhalation anesthesia, an embolus of phlebitic origin or an infection originating in an injected operative field and disseminated by the blood of lymphatic circulation, and that other postoperative pulmonary complications, occurring in cases in which operation is done with strict asepsis in an uninfected field and under anesthesia other than inhalation anesthesia, are due to the fact that every operation produces some toxemia because of breaking down of the proteins of the tissues by the operative traumatism and dissemination of these products by the venous route The toxic substances are chiefly

polypeptids The resulting toxemia differs from that due to heterogeneous proteins which accompanies shock and may cause visceral, including pulmonary, lesions

In attempts to reproduce this condition in animals, dogs were used and the polypeptids injected were obtained from the muscles of dogs The polypeptids were injected into both the saphenous and the mesenteric veins because in some operations only the peripheral veins are involved while in intra-abdominal operations the portal circulation is also affected Some of the experimental animals were sensitized by a preliminary subcutaneous injection of the polypeptids in a dose of 10 cg per kilogram of body weight Others were not so sensitized All of the sensitized animals developed pulmonary lesions whereas the non-sensitized animals showed no visceral lesions Controls anesthetized and killed in the same way showed no pulmonary lesions

The pulmonary lesions appeared as deep-violet-red areas which were clearly distinguished from the normal lung tissue. They varied in extent and distribution. Histological examination showed them to be of two types. (1) "pulmonary apoplexy" or infarction without obliteration of the blood vessels, and (2) typical pulmonary atelectasis or collapse of the lung. They resembled the lesions in clinical cases of postoperative lung complications in which death occurred soon after operation.

In one case on whom an exploratory laparotomy under local anesthesia was done, pulmonary complications followed, resulting in death after four days. The pulmonary lesions were the same as those observed in the experimental animals injected with polypeptids after sensitization. Blood analysis two days before death showed that polypeptids

were present in almost three times the normal amount, 80 mgm. The blood urea was two gm. This confirmed the experimental findings with regard to the relation of an increase in the polypeptids of the blood in the development of pulmonary lesions after operation

PNEUMONIA

Types of Pneumococci in Sputum of Patients with Pneumonia—N. I. Nissen²⁴ tabulated 192 strains from the sputum of patients with croupous or bronchial pneumonia out of 300 type-identified strains. The predominating types were I, present in 359 per cent, VII in 104, III in 94, VI in 73, IV in 52, and VIII in 47 per cent

In rubiginous sputum from 83 patients, pneumococcus types I, VII, IV, and III, were most frequent, typespecific agglutinins in the blood were established with rising and falling titer in the cases in which types I, IV and VII appeared in the sputum

Massive Atelectatic Collapse of the Lung Complicating Pneumococcus Pneumonia—M Finland and H I L Loverud ²⁵ In 62 cases of primary pneumococcus lobar pneumonia, this complication was shown by x-ray In another group of 47 cases of pneumococcus pneumonias, atelectasis of varying extent and due to a variety of factors was present at autopsy

Atelectasis is a very significant complication and the possibility of it should be borne in mind in cases of lobar pneumonia and may serve to explain certain otherwise puzzling physical finding, sudden attacks of dyspnea or an unusually protracted course

The usual course of events in the characteristic case where the atelectasis complicates convalescence is somewhat as follows. A patient, acutely ill with

typical lobar pneumonia, begins to show gradual signs of improvement such as lowering of fever and pulse rate and the appearance of moisture in the consolidated lobe indicating resolution. He is suddenly seized with intense dyspnea of short duration after which pleuritic pain, moderate fever, and leukocytosis recur, and the physical signs and x-ray give evidence of elevation of the diaphragm with a shift of the heart, and usually the trachea also, to the affected side consolidated lobe may then show signs suggesting fluid or these signs alternating with those of solidification When the upper lobe is collapsed, the breath sounds are intense and amphoric in character and, as moisture appears, suggest tuberculosis with cavitation These signs may be present while fluid accumulates in the pleural cavity. The collapsed lobe re-expands within a few days or weeks but organization and fibrosis may leave this affected lobe contracted

In certain patients, particularly if they are markedly prostrated after a severe course, the signs of collapse may appear during convalescence without an explosive onset

Collapse of varying degrees occurring during the acute stage of pneumonia may be manifested only by the signs suggesting fluid or by the evidence of displacement of the heart and trachea, or only by careful roentgenographic examination. In such cases, the collapse, if it involves the affected lobe, is usually of short duration, evidence of solidification soon appears, and the course of the disease continues. If a previously uninvolved lobe is collapsed, the disease may extend to involve this lobe.

Significance of Bacteremia in Pneumococcic Pneumonia - R C Tilghman and M Finland²⁶ consider 1586 cases of pneumonia associated with specific pneumococci of types I to

XXXII (Cooper), in which cultures of the blood were made during the acute stage of the disease or at necropsy. For each type the death rate in the cases in which the blood cultures were positive was two or more times as high as in the cases in which the blood cultures were sterile, and for all types it averaged almost three times as high. Positive results of blood cultures were obtained in slightly more than a third of all the cases. The incidence of bacterenia varied widely in the cases of different types and due to type II pneumococci.

In the fatal cases the incidence of bacteremia was four times as great as in the nonfatal cases, and this proportion was even higher when the cases in which serum treatment was given were ex-The mortality rate increased cluded progressively with the ages of the patients this being true for patients both with and without bacterenna. The greater mortality for bronchopneumonia was found for each type, both with and without bacterenna Bacterenna, however, was less frequent with most types of atypical pneumonia. The death rate was higher in the cases in which the greater amount of lung was involved. There was little difference in the incidence of bacteremia and in the death rate for nonusers of alcohol and for habitual drinkers

There was a significantly greater incidence of bacterenia in the cases of pieumonia which occurred in the course of other serious conditions or diseases (so-called secondary pneumonia) than in the cases of primary pneumonia

The differences in the mortality rate at different leukocyte levels varied in the same manner as the incidence of bacteremia. Bacteremia was most frequent in the cases in which the leukocyte count was below 10,000. It was higher in the cases in which the count was 35,000 or

more than in those in which it was between 10,000 and 34,000.

Bacteremia was more than twice as frequent in the cases in which there were postpneumonic complications as in those in which there were none. Conversely, the complications were more than twice as frequent in the cases of bacteremia as in the cases in which bacteremia was not noted.

In the cases in which no specific serum was given, the termination of the acute disease by crisis, lysis, or death, occurred most frequently between the seventh and the ninth day. Sterilization of the blood stream without apparent improvement of the acute symptoms or in spite of progression of the pulmonary lesion occurred more frequently after serum therapy was given than in cases in which no serum was administered

For the bacterenic patients who recovered, the colony count was usually below ten per cc of blood. The prognosis was usually, but not invariably, found to be unfavorable when the number of colonies increased in successive blood cultures.

Serum Treatment of Croupous Pneumonia—N I Nissen²⁷ states that the mortality in 74 cases of croupous pneumonia treated in 1934 and 1935 was 41.9 per cent. During the following 18 months, 100 patients were treated. Ten (or 16.9 per cent.) of the 59 given serum treatment died, and 23 (or 56.9 per cent.) of the 41 who received no serum died.

It is justifiable to treat every patient presenting croupous pneumonia with type I serum immediately on admission and until type determination is made, when treatment with type-specific serum should be continued

Antipneumococcus Rabbit Serum as a Therapeutic Agent in Lobar Pneumonia—F L Horsfall, Jr, K Goodner, C M MacLeod, and A H Harris, 2d²⁸ found pneumococci bac-

teremia present in 12 of 22 patients with lobar pneumonia, consolidation of two or more lobes in seven, bilateral consolidation in three, and pleural exudate containing large numbers of pneumococci in three.

The patients, ten with type I, four with type II, three with type VII, and five with type VIII pneumococcus pneumonia, were treated with unconcentrated type specific rabbit antipneumococcus serums.

Twenty-one patients recovered and one died of rupture of the aorta five weeks after the onset of the disease Recovery was rapid and by crisis in almost all, the signs of intoxication disappeared shortly after serum therapy Crisis occurred after an average of 26 hours following the institution of serum therapy, and latterly in five cases with the more rapid administration of serum, this period has been decreased to an average of nine hours

Empyema did not develop in two patients with grossly infected pleural exudates. Type specific antibody of rabbit origin was demonstrable in these exudates after the intravenous administration of serum, and following this the pneumococci disappeared. Empyema occurred in one patient. In this case type specific antibody was not demonstrable in the exudate and the pleural infection progressed, necessitating surgical dramage.

From these results it appears that unconcentrated type specific antipneumococcus rabbit serum in the treatment of lobar pneumonia is at least as effective as concentrated horse serum. This fact added to the relative rapidity and ease with which it can be produced, the low cost of the finished product, the facility with which it can be administered, as well as the evidence indicating that rabbit antibody can penetrate the pleura and assist in the sterilization of an in-

fected exudate would suggest that type specific antipneumococcus rabbit serum is a therapeutic agent of considerable promise.

Quinine Treatment of Pneumonia—E Ballmann²⁹ points out that the injection of *quinine* permits an energetic attack of the cause of pneumonia without disturbing and moving the patient. In a hospital, more than 2000 patients were given injections of quinine preparations and the number of cases in which complications developed was small

Injurious effects of the injection of quinine preparations, which have been reported in the literature, could have been avoided if the necessary caution had been observed Cases in which brachial nerves were paralyzed had been injected in the arm by inexperienced assistants or nurses Quinine preparations should be injected into the gluteal muscle only with a sufficiently long needle by the physician himself If these rules are observed. the treatment of pneumonia with quinine injections is without danger and, compared to the merely symptomatic treatment, it shortens the disease process and reduces the number of complications and the mortality rate

Insulin Therapy in Pneumonia of the Aged—S N Sinelnikov 30 regards pneumonia as a state of nondiabetic pathologic acidosis running a course characterized by a pronounced anoxemia with a considerable increase in the blood sugar, increased breaking down of albumin and fat, and marked lowering of the chloride metabolism. Achard was the first to refer to *insulin* as an alkalimizing agent, and Kogan-Yasnyy was the first to apply it in the treatment of pneumonia.

The blood sugar of the pneumonia patients was found to vary between 0 120 and 0 160 at the peak of the temperature curve. With the fall of the temperature,

the blood sugar content was from 0.09 to 0.08 per cent

The chlorides at the height of the disease varied between 0.58 and 0.6, during the crisis from 0.93 to 6.8, and several days after the crisis from 8.8 to 12

Insulin was administered twice daily in doses of from 0.5 to 1.5 Gm. One hundred twenty-two cases of croupous and of bronchial pneumonia were treated by this plan without a fatality. In a specially selected group of 18 elderly patients, there was not a single fatal issue

Four cases in which insulin therapy did not prevent death, at necropsy, showed complications of carcinoma, active tuberculosis, infarct of the left lung, and a ruptured aortic aneurysm, respectively

Blood Transfusions in Primary Pneumonia—J M Arena³¹ reports that during the last three years efforts were made at the Duke Hospital to give one or more blood transfusions to all intants and children who had severe primary pneumonia, whether or not they had anemia. However, because of the difficulty in obtaining suitable donors, 35 patients did not receive blood and consequently served as controls.

The other 24 patients had one or more transfusions of citrated blood by the gravity method (maximal amount 20 cc per kilogram of body weight)

The clinical symptoms, hemoglobin content and red and white blood cell count for the two groups were almost identical. The only difference which could be noted was that in the group who received transfusions there were probably more ill patients and more infants.

Prompt and marked symptomatic improvement usually followed the transfusion, and the patient appeared more comfortable. The temperature fell by crisis within 24 hours of the transfusion

in 15 cases and within 48 hours in the other nine. The average interval between the onset and the crisis or lysis for this group was $7\%_{10}$ days

Four of these children had the complication of suppurative otitis media, and one died

For the 35 patients who did not receive transfusions, the average interval between the onset and the crisis or lysis was $9\%_{10}$ days. Three of these children had the complication of empyema, and nine had otitis media. Five died. The severe dyspinea and cyanosis which many of these children had were improved instead of made worse by the transfusions.

Possibly, transfusions stimulate an increase in segmented polymorphonuclear leukocytes. The hemogram studies which have been made for several patients with primary pneumonia indicate that improvement or a crisis is attempted by an increase in the segmented polymorphonuclear leukocytes, with a decrease in the percentage of nonsegmented forms. The ratio of segmented to nonsegmented forms appears to be a good indication of the severity of the infection and the ultimate outcome.

Perhaps transfusions are a form of serotherapy, introducing neutralizing antibodies or causing nonspecific protein shock. Another factor may be the supplying of cells to carry needed oxygen to the tissues, the replacing of those withdrawn from the circulation by the pathologic process.

Parenteral Liver Extract Therapy in Pneumonia—J A Wilson and W C Carey³² treated 30 cases of pneumonia with parenteral liver extract. These included eight cases of streptococcic pneumonia and one of staphylococcic, in the remainder the pneumococcus was most frequently found to be the causative organism

Five of the 30 patients died All had pneumonia with a leukopenia or falling leukocyte count; three had pneumonia occurring in the course of a streptococcic septicemia, and two of these were the only patients to receive serum. They were given polyvalent antistreptococcus serum intravenously. No antipneumococcus serum was used.

A leukocyte count of more than 15,000 was present in only eight cases at the beginning of the treatment, the rest were below 15,000

The rationale of the use of parenteral liver extract therapy is as follows Parenteral liver extract stimulates leukocytosis, in some pneumonias, the blood picture is characterized by a relative leukopenia or a falling white blood count, these cases offer a more unfavorable prognosis, therefore, parenteral liver extract given in these cases should stimulate leukocytosis and as a secondary effect improve the clinical picture and progress

The concentrated liver extract was injected intramuscularly in varying amounts, depending on the severity of the infection and the leukopenia developing during the course of the disease. The injections were made deep into the muscles of the buttock and deltoid regions The average amount was 6 cc a day majority of the patients were kept in oxygen tents as long as dyspnea and cyanosis were present. Expectorants, such as ammonium chloride were given Morplime and codeme were given for severe pleural pains. An effort was made to keep the fluid intake between 3000 and 4000 cc daily. Liquid and soft diet were given in small amounts frequently Whisky was prescribed in small amounts for elderly persons. No purgatives were allowed If constipation became marked, saline enemas were given

There was an approximate increase in leukocyte count of 70 per cent and the range was from 6 to 239 per cent. After an injection of concentrated liver extract, the leukocyte count gradually rises for seven hours and then gradually falls. All but six patients responded by an increase in leukocyte count. There was a daily drop in the white blood cell count until liver extract treatment was started.

Several patients showed a marked increase in urinary output the day after parenteral liver extract was given

Pain occurs at the site of the injection, but this is moderate and of short duration

Sulfanilamide in Type III Pneumococcus Pneumonia—J H L Heintzelman, P B Hadley, and R R Mellon^{3,3} treated nine cases of type III pneumonia with *sulfanilamide* and ten with no special form of treatment

These cases occurred from September to March, inclusive, and the majority were under observation during January

Treatment consisted of the oral administration of sulfanilamide, augmented in a few cases by intramuscular injections of prontosil. Owing to the late arrival in the hospital of some of the patients, the first administration of sulfanilamide was sometimes considerably delayed.

There was a general similarity between the two groups, although predisposing factors, complications, age and the like were somewhat more favorable to the treated group. Seven of the nine patients recovered and two died. In the other group of ten patients, two recovered and eight died.

The mortality rate for all patients not treated with sulfanilamide was 74 pcr cent, that for the treated patients, 22 pcr cent. Despite the fact that the number of treated type III cases is small and that the treated groups were somewhat favored by the factors of age incidence and by the absence of significant compli-

cating features, the nature of the difference in relative mortality in the treated and untreated groups appears to justify continued use of sulfanilamide in the treatment of type III pneumonia until a sufficient number of cases have been accumulated to justify a final judgment as to the efficacy of this mode of therapy

TULAREMIA

By EDWARD L BORTZ, M D

The brilliant researches of Lee Foshay¹ during the past several years have uncovered a mass of interesting and important data concerning tularemia. Reporting on 750 cases personally studied, he points out that tularemic pneumonia is not the chief cause of death from this infection and believes that the mortality and morbidity data now available indicate that tularemic pneumonia cannot possibly be the chief cause of death.

Septicenna due to Bacteria tularense is the chief cause of death from tularemia Pneumonic lesions are present in about 50 per cent of all fatal cases. Most of the cases of pneumonia that are associated with tatalities derive from the septicemia. The pneumonia that originates from the primary bacteremia does not become associated with fatalities until septicemia supervenes. At least 70 per cent of the cases of tularenic pieumonia do not result in death. The septicenna which causes most tatalities origmates from a secondary invasion of the blood stream. Tularemic sepsis, with its consequent miliary focal necroses, may be generalized or be limited to either the systemic or the pulmonary circulation. In this way, it is similar to miliary tuberculosis

Tularenia is particularly hazardous to patients with pre-existing coronary artery disease. Death may occur in these cases from coronary occlusion or acute myocardial failure during the initial acute

phase or during early or late convalescence. The surviving patient may suffer attacks of angina pectoris, coronary occlusion, and heart block for months or years after recovery from tularemia.

Persisting, progressive, tularemic lesions which ultimately involve important structures are infrequent causes of death late in the course of the disease

The third week of infection is the most dangerous period, and most deaths occur on the sixteenth day of illness. The disease is characterized by severe toxemia which appears seldom or never to cause death among patients who were previously healthy. Persons over 50 years of age tolerate the infection less well than younger individuals.

Four of every five deaths from tulaterna could be prevented by the early administration of serum therapy

Treatment—Although the causative organism of tularemia was isolated in 1912 by McCoy and Chapin, little progress was made for 22 years in the treatment of the clinical entity as stressed by Barthelme ²

In 1934, Lee Foshay, of the University of Cincinnati, published the first report on the use of **serum** prepared from goats for the treatment of tularemia. The results were so far superior to any previous method of treatment, that this serum therapy was further investigated. The duration of the disease was lessened from five to three months;

the adenopathy from four to two and a half months. The duration of the fever was unchanged and averaged approximately 26 days. The earlier the patient is given the serum, the better and shorter is the convalescent period. The optimal time for serum therapy is before the twelfth day of the disease. If tularemia infection is kept in mind, the diagnosis can almost always be made so that serum treatment can be begun before the twelfth day. Intradermal tests have been found positive in about 300 tests, failing only twice, where the patient was dying

Following the use of the serum there is a marked recession of fever, general malaise, and psychic disturbances, with a marked reduction in the size of the lymph nodes. Serum therapy prevents the establishment of chronic tularemia. The serum is given ordinarily by vein, in dosage of 1 ounce (30 cc.). Usually 1/2 ounce (15 cc.) is given on successive days. Some patients may require 2 ounces (60 cc.). The incidence of serum sickness may be lessened after it is more carefully studied.

Barthelme has used *metaphen* successfully in the treatment of tularemin For the mild cases, he gives 2^{1}_{2} drams (10 cc) of the 1 1000 solution intravenously every second day for three injections. The more severe cases are given 2^{1}_{2} drams (10 cc) daily for four doses, then every second day for three more

In no case was more than $2\frac{1}{3}$ ounces (70 cc) of the solution given There is no reason, however, to believe that larger doses cannot be given in tularemia, because in streptococcic infections as much as $3\frac{1}{3}$ ounces (100 cc.) in seven days has been used without any noticeable harm. The urine is examined daily for any apparent kidney damage.

No general reactions were noted following the use of metaphen and only one patient complained of discomfort at the time of injection Phlebitis almost invariably occurred at the site of the injection This may be fairly painful for 48 hours or more. In some cases, the same vein was injected four or five times without any permanent occlusion The mortality rate for Barthelme's series was 17 per cent The duration of the fever in no case exceeded ten days after treatment was begun except in one case, where it persisted for 13 days. Eleven days was the average length of the fever before and during the treatment. The longest period any glandular swelling persisted was five weeks, whereas the average was 24 days The duration of the disease, that is, taking the time at which the individual was able to return to his former occupation without discomfort, averaged 32 days The longest any patient remained away from work was seven weeks. The lesion, even if tairly large, was mactically healed in two weeks

PULMONARY TUBERCULOSIS

By Frank Walton Burgf, MD

Ameloid Degeneration of the Adrenals was found by I D Bronfin and P H Guttman in 14 per cent of 100 cases of pulmonary tuberculosis that came to autopsy

Anacidity in 25 per cent and hypoacidity in 33 per cent of young tuberculous patients between the ages of 20 and 30 years was found in the gastric secretions by Gray and Melnick

Tuberculin has been purified and the active protein principle put in a form having the essential requirements of specificity, high potency, constancy in strength and stability by E. R. Long and his coworkers

Artificial pneumothorax maintenance of at least five to seven years is recommended by P Dufault and A Laroche, who note that diseased tissue alone is incapable of re-expansion, irrespective of the duration of the collapse. This opinion is substantiated by surveys of re-expanded cases followed from two to ten years.

Phrenicectomy results viewed 213 to 7 years after operation, were not highly tavorable as viewed by O. A. Beatty, an experience very generally shared by Slavin, Ballon, Wilson, Singer, Graham, Thomas, and Harper, who have surveyed after sufficiently long clapse of time

Semb's extrafacial apicolysis has been noted to close apical cavities with great regularity and low mortality and continues to be more widely accepted throughout the world

trastric lavage of 622 children with positive tuberculin tests revealed microbacterium tuberculosis in 199 in a study made by Poulsen. Andersen and Lester in Denmark. The precedure has found general acceptance as one of merit in the early age group. Most cases showing tubercle were between three and four years of age.

Thoracotomy for tuberculous empyema has been devised by Floesser, which does away with any dramage tube Dramage through an orifice in the chest wall is maintained by turning in a skin flap and suturing it to the inner chest wall. Thus an orifice is produced, having a valve-like action which emits pus but tends to exclude air.

Expectoration for testing for tuberculosis may be obtained from patients who

swallow all their sputum, by having the patient cough, preferably in the early morning, with a laryngeal *nurror* held above the larynx Material can be recovered from the mirror for testing Flecks of yellowish secretion of pin head size are characteristic R C Cohen and W B Wood advise the method

Bilateral pneumothorax has special indications and contraindications according to Carmen

Indications

- 1 Limited progressive bilateral disease without cavitation
- 2 Bilateral cavitation, preferably the motheaten type
- 3 Reactivation of trouble in the contralateral lung
- 4 Uncontrollable hemoptysis in the opposite lung
- 5 ()ccasional pleurisy, with effusion in the opposite pleural space
- 6 Acute tuberculous pneumonia, when the process is not too acute and extensive

Contraindications

- 1 Limited progressive bilateral disease out cavitation
- 2 Targe thickened wall cavities that resist compression
 - 3 Extensive fibroses in both lungs
- 4 In successive bilateral pneumothorax when a large cavity in the initial lung resists compression
- 5 Extensive pleuritic adhesions. A satisfactory collapse can rarely be obtained in the presence of this difficulty.
 - 6. Low vital capacity, below 2000 cc
- 7 Patients above 40 or 45 years of age Viter the fortieth year is passed, the cardiorespiratory system fails to compensate well
- 8 Extensive extrapulmonary complications Tuberculous laryngitis is not a contraindication. It is usually very materially helped by stopping the cough
 - 9 Threatening cardiac decompensation
- 10 Extremely low vitality and marked toxemia

Etiology—Development of Tuberculosis in Adult Life—J A Myers, H S Diehl, R E Boynton and B Trach³⁶ report that in schools of nursing and medicine where the students come in contact with tuberculous patients, in the absence of an adequate technic for dealing with contagious disease there has in recent years been presented an opportunity to study the development of *tuberculosis* in young adults that is rarely equaled by animal experimentation

Since 1927 many students of nursing and medicine have been observed who have become contaminated with tubercle hacilli for the first time, the evidence of this contamination being a positive reaction to tuberculin which appeared after the student was exposed to tuberculous patients In many of these students there has been no other manifestation of tuberculosis as yet They are classified as having the first infection type of disease somewhere in their bodies, with the location undetermined. Among this group are some students in whom, after the tissues had become sensitized, lesions developed in such locations or to such an extent that they could be demonstrated by roentgenograms or other phases of examination. These subjects are grouped on the basis of the tuberculin reaction, the type of lesion that subsequently developed and other factors

Adults in whom the first infection type of tuberculosis develops, even with considerable involvement of the pulmonary parenchyma and regional lymph nodes do not require treatment in any form

The prevention of tuberculosis of the first infection type among young adults consists in protecting them from exposure to patients with communicable tuberculosis. For students of nursing and medicine this amounts to a strict technic for dealing with contagious diseases.

When the first infection type of disease occurs in the second and third

decades of life, it is just as benign as when it occurs in childhood.

Pathology — The tuberculous cavity that alternately expands and contracts is believed by A. Korol to be affected by the condition of the draining bronchus, temporary stenosis or partial obstruction of which results in ballooning of the cavity.

Diagnosis — Circular Lesion of Pulmonary Tuberculosis — C C Birkelo and J A Kasper 77 observed 60 cases of pulmonary tuberculosis, selected on the basis of their circular outline. While some of the circular lesions developed from originally diffuse tuberculous infiltration, others were circular at the time of the first observation. A small group included those which appeared to represent the final stage of a primary or childhood type of infiltration. It is felt that some circular lesions develop from first infection. The circular lesions may be divided into three groups

The first group includes the lesions that have been found to develop from diffuse infiltration. Such lesions are not entirely stationary and may undergo excavation. Most of them, however, show a tendency to become smaller

The second group includes the lesions that are definitely circular when first discovered. They may be single or multiple but in most instances are solitary lesions varying in size from 0.5 to 3 cm in diameter. Most of them are of uniform density and well defined in outline, they are definitely in the parenchyma. Occasionally they excavate and may cause a spread of the tuberculous disease. These lesions remain stationary for months and years and probably represent the well encapsulated type, which is least likely to become active.

The third group includes the receding stage of the childhood type of infiltration. At first the lesions of this group

were definitely circular, later they retrogressed without any collapse therapy

It would appear that the lesions of the second group require only periodic check-up. In the event that excavation should begin, the indication would be for some therapeutic intervention. Three cases showed evidence of excavation, while 36 remained inactive

The lesions in the first group represent incomplete healing with the possibility of incomplete encapsulation. Since the majority of 16 cases showed retrogression, it would be justifiable to conclude that their outlook for satisfactory recovery would be good and that one might expect eventual disappearance of the lesion or complete encapsulation.

For the third group, continued observation is a necessity

Intracutaneous Tuberculin Tests— J. L. Law and C. W. Cory is studied 732 children of low economic status who came from households distributed in towns throughout two-thirds of the state of Michigan

The behavior of purified protein detivative in its two standard test dose in comparison with three dilutions of potent old tuberculin in about 3000 tests shows that the purified protein derivative is uniform in its reaction, potent and reliable

The first strength of purified protein derivative (0.00002 mg) found more reactors than did old tuberculin in a dilution of 1 10,000 (0.01 mg), or about the same number of reactors as did old tuberculin in a dilution of 1 1000 (0.1 mg). The use of the second strength of purified protein derivative (0.005 mg) found more than seven times more reactors than did the administration of old tuberculin in a dilution of 1 1000 (0.1 mg), whereas the giving of the second strength of purified protein derivative found twice the number of

reactors revealed by old tuberculin used in a dilution of 1:100 (1 mg)

Tuberculin Testing with Purified Protein Derivative— J S Whitney and I McCaffrey³⁹ report on the results of a total of 85,709 group tuberculin tests with first and second strength tuberculin (purified protein derivative) among 56,688 individuals in 30 states and the District of Columbia

The adjusted percentage of positive reactors among the 56,688 persons was 47 per cent The adjusted rate was ten per cent higher than the nonadjusted rate because of the small proportion of adults and persons of foreign extraction included in the groups tested were fewer positive reactors proportionately among the six-year-old children tested than there were at any other Following the sixth year of life, age the trend of infection was generally upward at an average rate of more than one per cent for every year of life up to the age of 20 Adults, 20 years of age or older, evidenced 34 per cent more tuberculous infection than the total number of boys and girls less than 20 years

The percentage of positive reactors found among the 8276 persons reported to have had contact with tuberculosis was 542, whereas only 333 per cent of those with no history of contact responded with positive reactions to purified protein derivative. The infection rate indicated for the contacts less than five years of age was three times that for noncontacts in the same age group, but the proportion of positive reactors increased with age, generally at a more rapid rate among the noncontacts than among the contacts

The adjusted percentage of positive reactors for males was 48 3 as compared with 45 9 for females. There was a larger proportion of male than female

positive reactors to purified protein derivative at almost every age group *

The trend of infection among the Negroes increased with age up to the age of 20 at a faster rate than that among the whites

Of the 31,318 native-born Americans of native parentage, 27 6 per cent evidenced tuberculous infection, whereas 38 4 per cent of the 6674 native-born of foreign parentage, and 61 2 per cent of the 814 foreign-born responded with positive reactions

The Incidence of Tuberculous Infection in American College Students—E R Long and F B Seibert⁴⁰ report that during the year 1935 to 1936, 18,744 students in 20 colleges received completed tuberculin tests in which a strong standard dose of purified protein derivative was administered to all negative reactors to an initial small standard dose

Geographic variations in the incidence of tuberculous infection was found, with relatively high rates (from 40 to 60 per cent) in the East and Far West and low rates (from 20 to 30 per cent) in the Central states Excessive rates were tound in regions noted as resorts for tuberculous patients. As most of the students were residents of the general region of their college, the figures are believed to reflect the incidence of tuberculous infection in the population of those regions.

In the same average age, the rate of positive tuberculin reaction was higher in men than in women

Treatment

Collapse Treatment of Pulmonary Tuberculosis — C M F Sinding-Larsen⁴¹ presents a careful study of 1126 proved cases of *pulmonary tuberculosis* upon which some form of *collapse therapy* was attempted at Vejlefjord Sana-

torium, Denmark, from 1906 to 1932. This series included approximately 35 per cent of the total number of patients discharged during this period. Follow-up studies were made in every case

The best results were obtained from effective artificial pneumothorax. Yet these were relatively few as the procedure was primarily technically effective in only 40 of 1021 patients

Seventy-three additional good results were obtained as the result of intrapleural pneumonolysis. Intrapleural pneumonolysis was found to be of real value, but extrapleural plombage was highly unsuccessful

Diaphragmatic paralysis proved of very limited value

Thoracoplasties were done on 299 patients Of these, 253 had demonstrable cavities. In 132 of these, closure was obtained before discharge. The results in this group were only comparable with those of partly effective pneumothorax. These poor results were probably due to the inadequacy of the operative procedures. Accordingly, the Semb type of operation was recently adopted. This provides for a freeing of the apex of the lung in addition to the extensive resection of the upper ribs, and allows apicocaudal as well as lateral collapse of the lung.

Even with protracted treatment in private sanatoria, patients with cavernous pulmonary tuberculosis have a very poor prognosis if they do not receive effective collapse treatment in time. In order not to deny some patients their only chance of recovery, the indications for collapse therapy should be drawn less rigidly.

Artificial Pneumoperitoneum After Puerperium in Pulmonary Tuberculosis—U DeMichelis^{4,2} believes there are several factors that aggravate the evolution of pulmonary tuberulosis after the puerperium There are hemorrhages,

loss of organic, inorganic and hormone substances through lochia and lactation and the mechanical factor of the lowering of the diaphragm.

In a case in which this occurred, an artificial pneumoperitoneum was established Intraperitoneal insufflations of from 300 to 500 cc of oxygen were administered at intervals of six days for about three months. The symptoms of the disease rapidly abated and the general condition of the patient improved X-ray examination of the thorax showed elevation of the diaphragin

l'atients tolerate this treatment well

Pneumoperitoneum in Treatment of Pulmonary Tuberculosis — H G Trimble and B H Wardrip⁴³ noticed that although the amount of elevation of the diaphragm of the pregnant tuberculous patient may be only from 2 to 3 cm, it is apparently sufficient to be of benefit to pulmonary lesions. If the amount of elevation caused by pregnancy is of value, one can be quite certain that the amount obtained by the use of pneumoperitoneum will also be helpful because as much as two or three times this amount can be obtained

The greatest degree of collapse has been obtained by the use of pneumoperitoneum in conjunction with phrenic nerve paralysis

With the addition of subphrenic pressure by pneumoperitoneum, the paralyzed leaf of the diaphragm may rise sufficiently to reduce the volume of the lung to as little as one-third of its original volume. The amount of diaphragmatic use varies with the individual, but a rise to as high as the third interspace anteriorly on each side has been noted from pneumoperitoneum alone.

The elevation of the diaphragm was a little greater with the patient in the upright position, also, if the patient was on one side constantly, the uppermost hemidiaphragm was more affected Consequently, when pneumoperitoneum is used in conjunction with phrenic nerve paralysis, the patient is kept on his good side. This, of course, is contrary to the procedure when a patient is placed at postural rest or on a bolster

The technic of pneumoperitoneum is very similar to giving pneumothorax refills

To date, three far advanced cases have been made sputum negative. Cough and sputum have frequently been diminished and the patient made more comfortable. Cavities that have failed to close by any other available procedure have been closed by pneumoperitoneum. This is particularly true of basilar cavities. In one case, it was effective in closing a large subclavicular cavity which had been present for two years. The beneficial psychologic effect on these patients for whom previously there was so little to offer, has been marked.

Partial Resection of the Lower Scapula as an Aid in Compressing Apical Tuberculous Abscesses and in Conserving Vital Capacity-E Holman44 believes that when a partial thoracoplasty will suffice to produce collapse of an apical, tuberculous abseess, it is desirable to do it with conservation of the greatest amount of normal lung An effective temporary collapse can usually be obtained by a sufficiently radical resection of the overlying ribs, but unless the dead space so created can be obliterated, there will later be a partial re-expansion of the underlying lung. If enough ribs are resected, the scapula will fall in and maintain the collapse However, ordinaily excision of the posterior part of the ribs down through the seventh rib is required. If resection of a smaller number of ribs will allow for collapse of the involved area, then a further

removal of ribs to allow the scapula to fall in will needlessly sacrifice normal lung tissues. Also, if the scapula cannot fall in, its lower angle will ride on the underlying ribs and frequently cause localized pain and elevate the shoulder

A simple procedure to allow for adequate and permanent local collapse with sacrifice of a minimum amount of normal lung tissue, is subperiosteal resection of enough of the lower part of the scapula to allow it to fall in and fill the dead space created by the rib resection. An incision is made around the angle of the scapula, the attached muscles and periosteum are elevated, and the denuded bone is removed with rongeurs.

According to the patient's condition and the conditions found at operation, the scapula is resected at the first or second stage. As five ribs must ordinarily be resected to allow even the smaller sized scapula to fall into the dead space, this additional resection is usually carried out at the second-stage operation.

Active paradoxical movements of the mobilized chest wall are always a menace, and in cases in which the risk is great they may prove fatal. The falling-in of the scapula largely counteracts this danger, and in such cases further resection of the ribs and scapula may be indicated.

Blood Studies in Tuberculosis Before and After Thoracoplasty—G L Muller⁴⁵ analyzed and correlated blood studies, including the corrected sedimentation rate and leukocytic counts, to various factors in 47 cases of pulmonary tuberculosis, prior to thoracoplasty and six months after the operation

Patients with a favorable leukocytic index and with a normal or practically normal sedimentation rate before a thoracoplasty are likely to respond well to the operation Patients with marked ac-

tivity of the disease process, as revealed by the leukocytic index and the sedimentation rate. likewise respond well if the trend of the blood, as revealed by serial examinations, indicates progressive improvement before the operation. Patients who shortly before the operation show an increase in the sedimentation rate and the leukocytic index and a neutrophilic shift to the left on serial examinations do not derive the expected benefit from the operation and some are made definitely worse More reliable information is obtained by evaluating all factors combined than by the consideration of a single factor alone

A Control Group for Studying the End-Results of Thoracoplasty—An Analysis of the Course of Those Patients Refusing Operation—S O Freelander and S E Wolpaw⁴⁶ selected 153 patients, during 1932 to 1934 inclusive, in Cleveland hospitals and sanatoria for thoracoplasty—Eighty-five accepted operation and 58 refused it The remaining ten refused at first, but after from one to three years consented to operation

The decisions to operate were made and the operations were all performed by the same group of physicians

A follow-up study was made on 114 of the 125 surviving patients during the first three months of 1937

Forty-eight (57 per cent) of the thoracoplasty cases and only six (ten per cent) of the control cases were "closed," meaning they had persistently negative sputum, x-ray evidence of a healed or retrogressive lesion without evidence of cavitation, and absence of constitutional symptoms. The mortality among the thoracoplasty group was 14 per cent, that of the controls 26 per cent

When the intermediate results were combined with the extremes, 66 per cent of the thoracoplasty cases and only 17

| | Thora 85 | Thoracoplasties 85 Patients | | ontrols Patients |
|-------------------------|----------|--------------------------------|----|---------------------|
| | No | Per cent | No | Per cent |
| Able to work | 40ª | 47 | 9ь | 16 |
| Well but unable to work | 8 | 9 | 1 | 2 |
| Curing | 19 | 22 | 28 | 48 |

PRESENT FUNCTIONAL STATUS OF THE COMPLETE THORACOPLASTY AND CONTROL GROUPS

per cent of the control group were closed or improved. In 21 per cent of the thoracoplasty cases and 61 per cent of the controls the condition was worse, or the patient had died

The group was further divided into a "good chronic" group and into a "slipping chronic" group The term "good chronic" is applied according to the criteria of Brown and Sampson, to patients who had a cavity of 2 cm or larger, whose general condition was good and who over an observation period of several months, had a normal temperature and pulse, a good appetite, and no significant loss of weight, and were able to take some exercise Sputum might be present and contain tubercle bacilli Roentgenograms of the chest showed no evidence of a progressive lesion patients who failed to quality for this group were termed shipping chronics"

In the 'shipping chronic' group with 42 thoracoplasty cases and 26 controls, 43 per cent of the former and only four per cent of the latter were closed cases Fifty-seven per cent of the thoracoplasty cases and eight per cent of the control were closed or improved. The mortality was 17 and 35 per cent respectively. In 29 per cent of the thoracoplasty cases and 77 per cent of the controls the condition was worse, or the patient had died

In the "good chronic" group with 43 thoracoplasty cases and 32 control cases, 70 per cent of the former and 16 per cent of the latter were closed Seventy-five per cent of the control cases were closed or improved. The mortality was 12 and 19 per cent respectively. In 14 per cent of the thoracoplasty cases and 47 per cent of the controls, the condition was worse or the patient had died.

The functional status of the patients were termed "able to work," "well but unable to work," and "curing". The 'able to work" group includes all cases which are closed or improved, or have been unchanged in the control group, those in which the patients are able to work full or part time and are not undergoing treatment. The "well but unable to work" group includes cases which are closed or improved, but in which the patients are functionally incapacitated by diminished vital capacity, weakness, or fatiguability. The "curing" group includes all of the remaining cases

Without thoracoplasty the course of the disease in the "good chronics" is different from that in the "slipping chronics," but thoracoplasty notably improves the prognosis of each group, both as regard to the healing of the disease and in the restoration of work capacity Delaying operation in the case of the

a Sixteen patients (19 per cent) working full or part time

b Three patients (5 per cent) working full or part time

| | Thoracoplasties | | | Controls | | | | |
|-------------------------|-----------------|-------------------------|-------------|-------------|-----------------------------------|-------------|---------------------------------------|-------------|
| | Chro | ood nics'' tients | s" Chronics | | "Good Chronics" 32 Patients | | "Slipping Chronics" 26 Patients | |
| | No | Per cent | No | Per cent | No | Per cent | No | Per cent |
| Able to work | 27ª | 63 | 13b | 31 | 8c | 25 | 1 ^d | 4 |
| Well but unable to work | 2 | 5 | 6 | 14 | 1 | 3 | 0 | 0 |
| Curing | 6 | 14 | 13 | 31 | 15 | 47 | 13 | 50 |

PRESENT FUNCTIONAL STATUS OF THE "GOOD CHRONICS" AND "SLIPPING CHRONICS"

"good chronic" in the hope of spontaneous recovery is not justified

Vitamin C and Tuberculosis— C K Petter⁴⁷ administered vitamin C in a chocolate-malt-milk base. The preparation contains ¾ grain (50 mg) of chemically pure cevitamic acid and 7½ grains (05 Gm) of dibasic calcium phosphate in two heaping teaspoonfuls, or 20 (m. This amount was given three times daily in 7 ounces (200 cc) of milk. The preparation as given in milk supplied 150 mg of vitamin C daily and added 654 calories to the regular diets

Of the 49 adults treated, 30 showed definite improvement, in 12 there was no change, and seven were definitely worse, 21 children showed improvement in weight and general condition

Elimination of cevitamic acid was found to be below normal in cases of advanced tuberculosis and was brought up to normal by feeding this vitamin in the foregoing doses

Influence on Vitamin C on Sensitivity to Tuberculin and on Blood Sedimentation—F H Heise, G J Maitin, and S Schwartz⁴⁵ determined the influence of vitamin C on the blood sedimentation rate and the tuberculin

skin test in 30 tuberculous patients, six were used as controls. The urinary excretion of vitamin C was previously determined in each from a 24-hour specimen of urine. The sedimentation rates were determined immediately before the use of vitamin C and again after the final injection. Preliminary subnormal urinary excretion of vitamin C was demonstrated in 19 of those receiving added vitamin C and in all of the controls.

Of the 19 with preliminary subnormal urmary excretion of vitamin C, 47 per cent showed a significant decrease and ten per cent an increase in sedimentation rate following vitamin C injection, 43 per cent showed no change. Of five patients with previously normal vitamin Curinary excretion, none showed significant changes in the sedimentation rate after injection of vitamin C. No alteration in the sedimentation rate was observed in the six controls after a period of five days. It seems that in a large number of cases, a condition of hypovitaminosis C may influence the sedimentation rate

In the study of the effect of vitamin C on tuberculin skin sensitivity, 16 patients were given a test with sufficient tuber-

a Eleven patients (26 per cent) working full or part time

b Five patients (12 per cent) working full or part time Two patients (6 per cent) working full or part time

d One patient (4 per cent) working part time

culm to cause only a mild intradermic reaction; six of these patients were used as controls and received no cevitamic acid A distinct decrease in sensitivity to the same dose of tuberculin was found after the patient received cevitamic acid, and those receiving cevitamic acid responded less acutely to a retest with stronger tuberculin than did the controls The average increase in the 24-hour erythema readings in the controls was 351 sq mm, as contrasted with 76 sq mm increase in those receiving cevitamic acid At 48 hours the differences The observations were not so marked indicate that in the presence of saturation with cevitamic acid tuberculin sensitivity becomes less

Blood Transfusions in Treatment of Pulmonary Tuberculosis — Pierre Bourgeois, H. Gisselbresch and S. Commerson-Teyssier⁴⁹ observe that medical literature contains little information about blood transfusions in pulmonary tuberculosis. The few authors who have nothing but praise for this form of treatment are forcefully contraindicated by others.

Out of ten cases of hemoptysis, seven were improved by injecting small quantities in doses ranging from 50 to 150 cc and never more than 300 cc, even in schous cases. The results are superior to subcutaneous injections of oxygen. There was improved coagulation and lessened hemorrhages, and a distinct increase in crythrocytes, lymphocytes, monocytes and cosmophils and in the percentage of hemoglobin. The polymorphonuclears were decreased.

Transfusion is contraindicated in cachectic patients, patients with oscillating temperatures and those in whom the extent of their lesions rendered their case hopeless

The improvement is not always stable. The favorable effect after the first transfu-

sion may not continue after the successive transfusions Besides these somatic effects, there is always a good psychotherapeutic effect

Insatiable Pneumothorax — A S Tenenbaum⁵⁰ recommends Forlanıni's method for pneumothorax, which requires in the physician not only skill but the utmost concentration to avoid complications, one of which is insatiable pneumothorax in which the injected air unaccountably disappears

Among 25 such patients it was noted that the pleural exudation did not amount to more than four per cent, while the ordinary pneumothorax patients reached an exudation of from 50 to 100 per cent Insatiable pneumothorax is rare and can be diagnosed only after exclusion of partial ordinary pneumothorax. It is observed not only in incipient tuberculosis but also in rather severe cases

To change it into ordinary pneumothorax, air must be pumped in repeatedly and atropine must be administered. The mechanism of appearance of insatiable pneumothorax is still unknown and the diagnosis remains an open question.

Insatiable pneumothorax may be classified into three groups (1) Early (primary) and late (secondary, (2) genuine and spurious, which is divided into the masked and partial forms, and (3) that in which mistakes have been made in the administration of pneumothorax. Penetration of the lung by the needle and subpleural injection of air

Ligation of Pulmonary Veins in Pulmonary Tuberculosis—L K Bogush, ⁵¹ on the basis of 11 ligations of pulmonary veins, concludes that access to the root of the lung and ligation of the vein is technically quite feasible after resection of the cartilage and a portion of the third rib The operation does not present great technical difficulties. However, the ligation of a thick short venous

trunk intimately connected with the pericardium, the narrow operative field, the presence of scars and adhesions about the root, the cough reflex whenever the bronchus is compressed and the cardiac pulsations call for delicate manipulations

Complete ligation of the pulmonary vein in tuberculous patients does not produce serious alterations of any kind. In the presence of limited involvement there is noted, in the first days and months after the ligation, a lowering of the temperature, diminution of the cough and of the amount of sputum, improvement in the general condition and appetite, marked diminution of the catarrhal signs and decrease or disappearance of tubercle bacilli from the sputum

Pulmonary vein ligation is a justifiable surgical intervention in the presence of fresh lesions limited to one lobe and not marked by great destruction. In the presence of an extensive destructive process with copious expectoration and high temperature, vein ligation may be useful as a preliminary procedure to the operation of thoracoplasty in order to reduce the secretion, lower the patient's temperature and improve the general status

Far Advanced Tuberculosis, with Complications, Tuberculous and Non-Tuberculous — (Cocke⁵² H states that in cases of advanced tuberculosts regardless how extensive the discase or apparently hopeless the case, persistent effort and hearty co-operation at times achieve results gratifying beyond expectation. The decision as to treatment seems easy in the light of developments, but in the course of treatment of a given case it is impossible to predict what might have been the result had it been handled differently Immunity in tuberculosis is unreliable and is acquired only after much difficulty and effort tuberculosis problem, formerly defined as the problem of relapse, is also the problem of complication, tuberculous or otherwise

Recently, the tuberculous patient has been considered as a better surgical risk At times, apparently than formerly hopeless advanced cases may be helped by skillful operation; numerous tuberculous complications may be overcome or at least helped Diagnosis of such complications, even when searched for, is not easy and is often delayed for an apparently mexcusable length of time in spite of utilizing all the present best methods of diagnosis, and the end may be either failure or at least a respite of a few years for the patient and a compromise existence Early diagnosis and prompt proper treatment are a necessity The tuberculous patient is a menace to himself as well as his contacts, and it is important to make an open case a negative one as early as possible if any therapy is to be successful

There are no set rules for deciding the appropriate treatment, each case must be judged on its merits at the time when something must be done and the judgment must be flexible. Factors other than the physical ones must be considered, such as the patient's morale, his attitude towards his disease and its unhappy progression, his co-operation, and the spirit he puts into the cure, and his economic security and ability to continue along the proper lines. The patient must be seen as a whole, mind and soul as well as body.

The millennial era will be when all tuberculosis is found early, because always suspected and searched for, and is treated appropriately before the development of complications

Dissection of Pleural Adhesions under Pleuroscopic Control in the Course of Therapeutic Pneumothorax—E Leuret, C Nancel-Penard, and P Cluzel ^{5,3} Artificial pneumothorax is

necessarily incomplete if there are pleural adhesions that hold the lung fixed to the thoracic wall and prevent its complete collapse To remedy this condition, Jacobaeus proposed cutting these adhesions with the galvanocautery, under pleuroscopic control Jacobaeus devised a special pleuroscope for this operation, and used a galvanocautery with a platinum loop for cutting the adhesions Maurer and Gullbring modified Jacobaeus' pleuroscope and diathermy has been introduced for cutting the adhe-Matson uses diathermic electrocoagulation, or a cutting current, Maurer combines diathermic electrocoagulation with the cutting effect of the galvanocautery, using a combined cautery with which either current may be used, regulated by a system of pedals. In some cases, extrapleural detachment of the adhesion is done

From December, 1934, to July, 1936, 34 tuberculous patients were operated at the Sanatorium Xavier-Arnozan. In five only pleuroscopy was done and in 29 the adhesions were sectioned. General anesthesia with rectanol was used prevent bleeding of the tissues at the site where the meision is made for the introduction of the pleuroscope, a hemostatic fluid is applied to the skin around the meision and a 1 1000 adienalin solution is injected into the subcutaneous The Cullbring pleuroscope is used. In most cases, the combined use of diathermic coagulation and galvanocautery is preferred

Morphine or pantopon is administered after operation as the patient must not cough for 24 hours. In 48 hours the pressure in the pleural cavity is determined manometrically and if necessary an insufflation of air may be given, or a small quantity of air may be withdrawn it the patient is dyspneic. Later refills

are carefully made to re-establish the pneumothorax

In 468 per cent of the cases, pleural effusion developed after operation, but in most cases the effusion was nonpurulent and was absorbed rapidly. The effusion 15 probably a reaction of the pleura to the irritation of the operative procedure.

Permanent good results were obtained in 16 (65 5 per cent) of the cases, temporary good results in three cases, and no improvement in three cases. There were seven cases with postoperative complications, including two with perforation of the lung, two with hemorrhage, two with postoperative symphysis and purulent pleurisy involving loss of lung tissue, and one case of purulent pleurisy

Postoperative complications may be attributed partially to faults in technic and also to a poor selection of cases. One of the cases of perforation of the lung, which was fatal, occurred in a febrile patient with bilateral pneumothorax. It is dangerous to attempt operation in a case of this type.

The chief indication for the use of this procedure in the tuberculous patient in whom artificial pneumothorax has been established is incompleteness of the pneumothorax as indicated by (1) Persistence of positive sputum, (2) persistence of a cavity distended by the adhesion as shown by x-ray even if the sputum is negative, (3) persistence of signs of activity, such as fever and failure to gain weight. The pressure of a pleural effusion may also be an indication for operation

The best time for operation is from the second to the fourth month of the pneumothorax, best results having been obtained in cases operated upon in the second month

Thoracoscopic Examination and Cauterization of Adhesions — P V Benjamin⁵⁴ believes that every patient treated by artificial pneumothorax for

whom x-ray examination after the first six or eight weeks shows the lung is collapsing imperfectly, is a potential subject for thoracoscopy and cauterization of adhesions

The presence of adhesions alone is not always an indication for operation. Some adhesions do not prevent a satisfactory collapse. Whether a collapse is satisfactory or not can be judged by the effect of the pneumothorax on the clinical symptoms, such as temperature, cough, the quantity of sputum and the presence of bacilli, and also by the changes in the blood

In some cases, although the patient improves under treatment by pneumothorax in spite of the presence of adhesions, cauterization may have to be done eventually if the adhesion shows a tendency to pull out the lung too early

There must be sufficient pneumothorax space for the manipulation of the instrument. If effusion is present, the fluid has to be aspirated before cauterization. A recent acute onset of effusion is a definite contraindication, and thoracoscopic examination should be postponed until the acute stage is over as manipula-

time of the operation and disappeared after the operation from the sputum of six. In the remaining 30 patients, all the adhesions that were seen could not be cauterized but one or more adhesions were cauterized in every case. As a result of the operation, the collapse of the lung was increased in all. Twelve patients were much improved and nine improved, making a total of 21, or 70 per cent, positive results

Tubercle bacilli were present in the sputum of the 30 patients in this group at the time of operation, and they disappeared from the sputum of 14, or 467 per cent, after the operation

Internal Pneumolysis—F G Chandler performed 110 consecutive operations during the years 1929 to 1934 (not including cases of bronchiectasis) on 89 patients. The youngest was seven years, the oldest 54 years. In January, 1936, their condition was as follows.

| In good health | 47 |
|-------------------------------|----|
| In fair health | 11 |
| Not robust or had had relapse | 6 |
| 111 | 3 |
| Dead | 15 |
| Untraced | 7 |

| | Times met | Times met Method | |
|--|---------------|------------------|--------------|
| Comply good on band | with 23 | One cannula | I wo cannula |
| Single cord or band Two to three adhesions Four to six adhesions More than six adhesions | 32 46 9 | 25 32 3 | 7 14 6 |
| | | 75 | 35 |

tion inside the pleura at this stage is likely to cause severe reactions

In only 10 of 40 patients could all the adhesions be cauterized. Collapse of the lung was increased in these ten after the operation, five were much improved and two improved. Tubercle bacilli were present in the sputum of the ten at the

Mechanical results

| Complete collapse | 49 |
|---|-----|
| Greatly improved collapse | 17 |
| Closure of cavity without complete col- | |
| lapsc | 1() |
| Unsatistactory collapse | 13 |

It has been suggested that diathermy (D) is more apt to produce an effusion

than the electrocautery (E C.). The differences in the following figures are probably of little or no significance as the electrocautery alone was used only for the easier and nonvascular adhesions

| Type of current | Times employed | Fluid appeared |
|-----------------|----------------|------------------|
| EC alone | <i>2</i> 8 | 4 (14 per cent) |
| D alone | 35 | 8 (23 per cent) |
| D and EC cor | nbined 47 | 12 (25 per cent) |

Empyema occurred seven times

| Tuberculous | | 3 | cases |
|-----------------|-------|---|-------|
| Mixed | | 3 | cases |
| Staphy lococcus | albus | 1 | case |

SECOND SERIES

One hundred operations were performed on 68 patients between 1934 and 1936, all tuberculous cases. The youngest patient was 16 years and the oldest 49

Present condition

| In good health (TBO) | 40 |
|------------------------------------|----|
| In tair health | 11 |
| Relapse or extension to other side | 7 |
| Very ill | 3 |
| Dead | 1 |

Adhesions varying from simple bands to complicated systems of adhesions, sometimes more than 4 mehes in width and 2 or more inches in thickness.

| Single I wo to three I our to six More than six | 10 cases 19 cases 19 cases 15 cases |
|---|--|
| Technic | |
| 2 Instruments | 3 times |
| 1 instrument | 97 times |
| Electrocautery alone | 4 times |
| Diathermy and electrocautery | |
| combined | 96 times |
| Mechanical results | |
| Complete collapse | 31 cases |
| Greatly improved collapse | 30 cases |
| Closure of cavity without | |
| complete collapse | 4 cases |
| Unsatisfactory collapse | 4 cases |

| Pleural effusion, following ope | eration |
|----------------------------------|---------|
| Slight (just covering diaphragm) | 8 cases |
| Moderate | 2 cases |
| Much (more than 1/2 up chest) | 2 cases |

Later effusion (occurring some weeks after operation)

| Slight (just covering diaphragm) | 12 | cases |
|----------------------------------|----|-------|
| Moderate | 9 | cases |
| Much (more than 1/3 up chest) | 4 | cases |
| Obliterative pleurisy | 5 | cases |

Surgical emphysema

| Slight | . 27 | times |
|----------|------|-------|
| Moderate | 4 | tımes |
| Much | 4 | tımes |

Temperature reaction

| 61 | times |
|----|---------|
| 31 | tımes |
| 5 | times |
| 3 | tımes |
| | 31 5 |

Empyema—1 case of tuberculous empyema occurred four months after operation

Hemorrhage—Oozing occurred in one case and was easily controlled by diathermy

Artificial Pneumothorax with Particular Reference to the Ambulatory Patient—J A Myers ⁵⁶ Modern methods of diagnosis have made it possible to detect progressive chronic pulmonary tuberculosis in the presymptom stage when the patient is in good general health, and often before tubercle bacilli are being disseminated to others. Therefore, more patients are being found who are the best subjects for treatment by means of artificial pneumothorax.

When artificial pneumothorax can be successfully administered in the ambulatory patient, it embraces the three essentials in the treatment of pulmonary tuberculosis (1) Checking the spread of the disease, (2) conversion of positive to negative sputum, and (3) restoration of the patient's working capacity in the shortest possible time

When the disease is found in the early stage and is known to be progressive, artificial pneumothorax should be instituted at once. Bed rest alone permits the progression of the disease in far too many patients to justify its exclusive use. In all patients with unilateral progressive disease in the moderately or far advanced stage, artificial pneumothorax should be attempted, provided there is no special contraindication

In most patients with early unilateral tuberculosis, many with moderately advanced unilateral disease, and some with far advanced unilateral disease, artificial pneumothorax may be safely undertaken on the ambulatory basis, that is, with no period of strict bed rest up to a period of three months of bed rest

Carefully administered artificial pneumothorax on the side of the more extensive lesion may be of great benefit even when bilateral disease is present. In some instances, partial bilateral pneumothorax is helpful. When a lesion makes its appearance in the contralateral lung which was previously clear, and shows evidence of progressiveness, treatment may be discontinued on the side of the original disease provided it is well controlled, otherwise, bilateral artificial pneumothorax may be indicated

In no patient whose cavities are not adequately closed after artificial pneumothorax has been given an adequate trial, should this treatment be continued because of the danger of spreading the disease to the opposite lung and the risk of hemorrhage and empyema. The treatment should be discontinued and surgery should be used.

Pneumothorax Treatment of Tuberculosis—R K Childerhose⁵⁷ states that it is generally agreed that *collapse* should be maintained for at least three years. Some advocate from five to six years

Just because a lung is well collapsed, the patient is not necessarily able to work. Unfortunately, there has developed in recent years a careless habit among physicians to permit exercise, usually in the form of work, during the period when the disease is still active. This tendency cannot be condemned too strongly. The disease can advance easily in the lung even if the lung be well collapsed, and unless the body receives the generalized rest that is so much required, grave risks are being courted

It is a good plan to consider the pneumothorax patient as a bed patient for the first six months. This does not necessarily mean a strict bed rest, but the patient should not be permitted any great exercise. Usually the patient is able to perform part-time work during the second year of treatment and full-time after that

The x-ray under collapse therapy is of small value in determining the degree of healing, and the amount of exercise may be governed by the blood sedimentation rate

Re-expansion of the lung should be done just as carefully as collapse patients with extensive destruction by cavities, there is danger in attempting to re-expand the lung too quickly. In these cases it is naturally impossible for the lung to completely hypertrophy by a compensatory emphysema and refill the original space. The extensive degree of fibrosis that forms in the long period of collapse precludes such a possible expansion and as a result the mediastinum is drawn well to the affected side, giving rise to some of the most extreme cases of mediastinal shift. In cases in which the mediastinum has become thickened and stiffened by the presence of a pleural exudate, this shift is not noticed to nearly such a degree and, therefore, a high degree of tension is exerted on this fibrosis Consequently, there is always the possi

bility of reopening the well-fibrosed lesion. To lessen this danger, a phrenic neurectomy is sometimes done which by releasing the diaphragm upward, will lessen the space to which the lung must re-expand.

During the period of re-expansion, there is a tendency for the formation of a moderate pleural effusion, which because of thickened pleura will not absorb, and must be aspirated to facilitate the re-expansion of the lung

Artificial Pneumothorax in Bilateral Pulmonary Tuberculosis-B Z Bunina, A O Gurevich, M P Rosenoer, and A. D. Kulikov58 report observations on 219 patients with an active bilateral pulmonary tuberculosis treated either by a unilateral or by a bilateral artificial pneumothorax and observed for a period of six years. In 60 of the cases, unilateral pneumothorax was induced. The theory of bronchogenic aspiration in the genesis of the development of the tuberculous lesions in the lung opposite the collapsed lung, is rejected Study of serial roentgenograms show that the new too in the opposite lung develop on the basis of pre-existing lesions

Thirty-eight per cent of the patients with infiltrating lesions were rendered bacillus free as the result of treatment with unilateral artificial pneumothorax, and the same effect was noted in 32 per cent of the cases in which there were disseminated foci

Sixteen of the 60 patients treated by unilateral pneumothorax developed pneumopleuritis. Twelve of these were cases presenting caseating lesions.

Recent infiltrating lesions with a more or less extensive involvement of the opposite lung without, however, clinically or roentgenologically demonstrable destructive lesions are best treated by a unilateral pneumothorax. Induction of

artificial pneumothorax on the opposite side is indicated when the lesions there begin to show signs of breaking down. The collapse should not be postponed long. Simultaneous bilateral induction of artificial pneumothorax is indicated for cases exhibiting a recent infiltrating bilateral process with a tendency to break down or with disseminated foci and cavities. In cases in which there are recent bilateral lesions and marked predominance in one lung, one may commence with a unilateral pneumothorax.

Collapse Therapy in Pulmonary Tuberculosis—G L Leslie and R S Anderson⁵⁹ give the final results of an intensive collapse therapy program for 1124 patients of a single large sanatorium, including 823 discharged and 301 resident patients

Collapse therapy in some form was instituted in 723 per cent of the discharged patients. It was recommended in 81 per cent of the entire series and was actually used in 788 per cent

Of 823 discharged patients, arrest or apparent arrest of the tuberculosis was secured in 47 3 per cent, favorable results in 671 per cent, cavity closure in 57 per cent of cavity cases, closure or decrease in the size of cavities in 69 6 per cent, sputum conversion in 59 per cent of the positive cases and negative sputum in 707 per cent of the discharged patients, of whom only 286 per cent had negative sputum throughout the entire period of treatment Of 595 discharged patients who received collapse therapy, the figures for similar results were invariably much higher, being respectively 55 4, 77 8, 71 3, 84 2, 72 7 and 79 3 per cent Corresponding figures for cavity and sputum results for the entire series of patients were usually slightly higher than the foregoing figures for the discharged group alone

A comparison of these results with those of a large number of sanatoriums using relatively little collapse therapy as an average clearly shows that the former are vastly superior from every point of view. The results constitute an overwhelming argument in favor of a definite policy of early and intensive collapse therapy for approximately three-fourths of the patients with the adult type of tuberculosis in the civilian sanatoriums of this country

Complications

Observations on Larynx in Tuberculous—F P Schuster⁶⁰ studied the larvnx in 562 cases of pulmonary tuberculosis with subjective symptoms referable to the ear, nose or throat Tuberculous laryngitis was present in 192 per cent of the cases This incidence is somewhat higher than would be expected in the mere routine examination of the larynges of tuberculous patients, without subjective complaints

Diseases of the nose and throat were no more frequent in patients with tuberculous laryngitis than in those in whom the disease was limited to the lungs The pathologic picture is essentially that of tuberculosis elsewhere and is extremely protean, more than one type of lesion occurring in the same larynx and frequently complicating secondary nontuberculous lesions

Subjective symptoms are of little diagnostic value, and the diagnosis is based on the gross observations in the larynx, with the confirmatory observations in the chest and results of laboratory and x-ray study

Prognosis is good as to healing of the laryngeal lesion in the early stages but guarded as to ultimate recovery Early treatment is based on co-operation with the specialist in diseases of the lungs in the general care, on absolute rest of the

voice, on pulmonary collapse in suitable cases and on avoiding overtreatment locally Occasionally, reflected sunlight is of value in supervised cases. When the lesion is progressive, the radical and repeated use of the galvanocautery is of great value, care always being taken not to exhaust the patient at any one sitting. Time and temporary relief may be gained by blocking the superior laryngeal nerve. Early use of the actual cautery is urged, especially when the condition does not promptly respond to conservative treatment

Pulmonary tuberculosis is basically the primary focus of laryngeal tuberculosis Intelligent co-operation between the chest man and the throat man will result in striking results in the prevention, early diagnosis, and successful treatment of this serious complication

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NEUROLOGY AND PSYCHIATRY

I'dited by Bernard J. Alpers, M.D., and Kenneth E. Appel, M.D.

BRAIN ABSCESS

By Robert A Groff, M D

Treatment—The method of treatment in brain abscess up to the present time has been by incision and drainage after the abscess has been localized G Vincent, and M David,1 have proposed a method of complete removal of the encapsulated abscess en masse through an osteoplastic flap These authors report a series of seven cases in which they performed a cramotomy, exposed the abscess, removed it without rupture and closed the wound without drainage Six of the seven patients recovered and were apparently cured. The death of the one patient was not caused by infection.

The authors' first patient, with a history of cranial hypertension for six weeks, was operated upon November, 1934, after preliminary ventriculography. A large frontal craniotomy was performed and in searching for a tumor with a trocar, the abscess was entered Twenty cc of pus were removed The trocar was withdrawn and the wound closed After an uneventful convalescence, the wound was reopened in January, 1935, and the encapsulated abscess removed by the electrosurgical forceps Following the operation, marked cerebral edema developed and was controlled by dehydration and lumbar puncture No further complications developed and the patient was in excellent health eight months later

This, the first patient in their series, is said to be the first subacute abscess of the brain to be removed completely, except in the few instances where a chronic abscess mistaken for a tumor has been removed. The basis for this method of treatment is that the greater number of cerebral abscesses, when seen by the surgeon, have a thick wall and that after the abscess has formed, the

chief factor is increased intracranial pressure and not infection. During the stage of capsule formation, which takes from 15 to 20 days, the authors recommend a decompression to take care of the cranial hypertension. Vincent and David do not recommend this method in all cases but rather issue warning that drainage of cerebral abscesses should not be done indiscriminately.

A further report by the same authors and H Askenasy² recounts additional experiences in the treatment of subacute and chronic abscesses of the cerebral hemispheres by the same method. They state that repeated puncture and drainage is effective only in cases of small abscesses near the surface without any tendency to extension. This treatment does not succeed in abscesses deep in the hemisphere If the abscess has no well formed capsule and the patient's condition does not permit extirpation, a large osteoplastic flap should be done for purposes of decompression When sufficient time has elapsed for thick encapsulation, the wound may be reopened and the abscess removed en masse

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BRAIN TUMORS

By Robert A Groff, M D

Diagnosis—Three clinical signs are considered diagnostic of corpus callosum tumors by Brouwer and Biemond (1931) These are (1) marked psychic or mental disturbances, (2) fever and (3) xanthochromia J Michelsen¹ gives further support to this syndrome by a report of seven cases of corpus callosum tumor. In six cases the

tumor was seen at autopsy and in one at operation

All of Michelsen's patients had this triad of symptoms. The psychic disturbances are described as general catatonia, negativism and mania. Their pathogenesis is obscure. The corpus callosum connects the two cerebral hemispheres and it is reasonable to assume

that it also associates the conceptions and ideas taking place in the hemispheres. From the phylogenetic standpoint, the corpus callosum must possess some psychic function, since animals without this structure are psychically of a lower grade.

The cause for the increased temperature which these patients show is not understood The author states that it is not the result of infection and the corpus callosum has not been shown to have temperature regulating fibers The close proximity of the corpus striatum permits this structure to be invaded early by the tumor Injuries to the corpus striatum have been known to produce fever Although there is no way of telling whether the fever is the result of infection or central in origin, patients with infection show a general systemic reaction and increase in pulse and respiratory rate whereas the latter show none of these findings. Kroll has found that in patients with fever of central origin the skin temperature does not rise proportionately to that of the body as is the case in infection

Nanthrochromia was present in all the spinal fluid examinations. Along with this finding there was an increase in both the cell count and protein content. The reason given for these changes is the close relationship of the tumor to the ventricle.

B J Alpers² in a recent paper, feels that the mental changes are more or less specific for tumors of the corpus callosum and taken together, with other evidences of a space taking lesion within the skull, make a diagnosis possible

In a study of two patients, Alpers vividly portrays these mental changes. The intellectual sphere shows a distinct deficit which is featured by inability to concentrate, difficulty in thinking, and above all, by what may be called com-

plete imperviousness to stimuli of all sorts, particularly auditory stimuli In the milder cases this is revealed by an attitude of seeming indifference to all happenings in the external world In the more advanced cases the patient responds not at all to auditory impressions or his responses are not relevant. The changes in personality and psychiatric episodes which have been described in corpus callosum tumors are merely incidental They are the result, probably, of invasion of the frontal lobes and of increased intracranial pressure Personality changes may occur but probably are due to frontal lobe involvement. It must be remembered, however, that one must have those signs of increased intracranial pressure as demonstrated by examination of the eve-grounds and estimation of the spinal fluid pressure, indicating a space taking lesion within the brain before such mental symptoms can be ascribed to tumors of the corpus callosum

Roentgenographic signs indicative of an intracranial tumor are of three types according to M. C. Sosman³ (1) Signs of increased intracranial pressure such as increased convolutional markings, separation of the sutures and atrophy of the sella or the sphenoid wings, (2) localizing signs, such as localized thinning of the vault or base, increased vascularity in one area, or displacement of the pineal gland, and (3) localizing signs identifying the type of tumor, such as expansion of the sella turcica due to a pituitary tumor, or the characteristic bony spicules, increased vascularity, and changes in the bone overlying a meningioma

This report constitutes a review of films made on 939 patients. The author states that the diagnosis of the presence and location of an intracranial tumor was made more accurately by roentgenography, exclusive of encephalography

and ventriculography, than by the clinical methods used on the medical service. The neurosurgical service has a higher percentage of accurate diagnosis than was obtainable by roentgenography alone, but this service had the advantage of the roentgenogram. The x-rav examination revealed the location of the tumor in almost half the cases and the histological picture was diagnosed in one quarter of the cases In only four per cent of the cases was a false diagnosis of tumor made No evidence of an intracranial tumor was presented by the roentgenogram in 49 per cent of the cases.

As for the type and location of the tumor, 91 per cent of the verified pituitary tumors were correctly diagnosed by x-ray examination. Meningiomas were localized in 67 per cent and 53 per cent of the acoustic neuromas gave focal signs. Cerebellar tumors gave positive findings in the roentgenograms in 45 per cent of the cases and of the supratentorial gliomas, 46 per cent showed signs of localization or demonstrated calcification within the tumor.

Ventriculography was employed 116 times A verified tumor was found in 62 and in 95 per cent of these, the tumor was located correctly. The author feels that if ventriculography and roentgenography are used in each patient, all intracranial tumors of sufficient size to cause symptoms can be located. The exception to this generalization will be in those instances where the tumor is below the tentorium, and in the case of small tumors in and around the optic nerve or chiasm and in small pituitary tumors.

Treatment—Last year the report of C H Frazier and B J Alpers⁴ to the Association for Research in Nervous and Mental Diseases on the effects of *irradiation* upon 156 gliomas was summarized

This study was based upon all the available material from the various large neurosurgical clinics in the United States The cases included in this report had a pre- and post-radiation specimen of the tumor. It was clear from this study that the medulloblastoma is the most sensitive of all the gliomas to irradiation, but a definite response is shown also by the ependymomas and astrocytomas. A mild response is exhibited by the glioblastoma multiforme group and no response is shown by the oligodendrogliomas.

E M Deery⁵ gives his experiences with the results of irradiation, in a series of 50 cases, all or part of which were included in the report just mentioned above. He points out the difficulties in drawing conclusions in such a study and stresses the need for more exact standards in order to evaluate the results obtained.

Deery points out that no conclusions could be reached from the study of his material Examples are given in which in one type of tumor changes produced by the roentgen ray were either marked, moderate or absent The number of cases is too small and it is only by the study of a large group that one can hope to draw conclusions

Commenting upon the histologic changes seen, Deery states that the tumor cells show the most marked alterations Death of cells was often found with a decrease in the total number of tumor cells as determined by the actual cell counts. Areas of necrosis were more numerous than in the pre-radiation specimen Mitotic figures in general were less frequent following irradiation as determined by counts. At times postradiation specimens showed the appearance of an increase in giant cell forms.

The author expresses the opinion that the blood vessel and connective tissue

phenomena commonly seen in post-radiation material are secondary to either manipulation of the tissue at operation or release of intracranial pressure by the decompressive effect

X-ray Treatment — C A Elsberg, L M Davidoff, and C G. Dyke⁶ in an effort to overcome the usual effects of heavy irradiation to the scalp and bone and at the same time give brain tumors sufficient irradiation, have devised an ingenuous method of treatment. They irradiate the tumor through the open wound at the operating table.

Prior to the application of this method, a series of animal experiments were made. The cerebrum, cerebellum and spinal cord of monkeys (macacus rhesus) were subjected to irradiation. They found that a dosage of 5000 or more r units exerted an injurious effect upon the part treated. A dosage of 3000 r units produced no harmful effects over a period of four months after irradiation.

From this experience, 18 patients were given no more than 2500 to 3000 r

units at a target distance of 50 cm. In the medulloblastomas of the posterial cranial fossa, the tube was brought near the surface of the growth, all filters were removed and the kilovoltage lowered to about 100, to prevent penetration of the medulla by the rays Irradiation was given after as much of the growth as possible was removed and hemostasis had been secured The wound was covered with cellophane and about the wound were placed four to six layers of sterilized lead foil The authors state that as far as they could determine, no immediate effects occurred from the treatment

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CHOREA

By MINIEL SALL, MD

Relatively little advance has been made in the past year in diseases of the basal ganglia, of which chorea is an example. The treatment of chorea still remains an individual problem. Most of the mild cases react well to conservative treatment such as rest in bed, quiet, and mild sedation. More severe cases and recurrent cases are best treated with fever therapy (typhoid vaccine). Some clinicians advocate fever therapy even for the mild cases. This may be desirable in order to prevent future attacks of the disease. The use of nirvanol has been quite gen-

erally discarded since the dangers from use of the drug are so great. Recent experiences with anesthetics such as evipal and avertin are being watched with interest, but thus far there have not been enough cases treated with these drugs to warrant definite conclusions.

Treatment

Donald Weisman and Charles Leslie¹ report striking success in the treatment of 50 cases of chorea by the intravenous injection of *typhoid-paratyphoid vaccine*. New York City typhoid-paraty-

phoid vaccine or its equivalent is used This preparation contains 1000 million B Typhosus and 750 million each of B Paratyphosus "A" and B Paratyphosus "B" in each cubic centimeter. The lot number should be noted carefully; the same child should always receive the same lot number The initial dose is always 005 cc undiluted vaccine intravenously Tolerance to the vaccine increases with each day's treatment in the large majority of cases The dosage must be constantly increased in accordance with the previous reactions Thus, if the temperature goes to 105° F (405° C) with a dose of 005 cc, give 008 cc the next day, if 104° F (40° C), give 0 10 cc the next day, if 103° F (394° C), give 020 cc the next day After the first day, a second dose or even a third is given on the same day if the temperature with the first dose remains stationary for two consecutive readings at less than 104° F (40° C) This must be injected promptly when the temperature is leveled and before the temperature starts descending from the first injection Thus, with an initial dose of 020 cc if the temperature levels at 101° F (393° C), give an additional 020 cc, with an initial dose of 020 cc, if the temperature levels at 102° F (39° C). give an additional 0.15 cc, with an initial dose of 020 cc, if the temperature levels at 104° F (40° C), give an additional 005 cc Furthermore, if the temperature goes to 105° F (395° C) with 020 cc plus 020 cc, give 050 cc the next day as an initial dose, if the temperature goes to 104° F $(40^{\circ}$ C) with 0.20cc plus 020 cc give 055 cc the next day as an initial dose, if the temperature goes to 103° F (394° C) with 020 cc plus 020 cc, give 060 cc the next day as the initial dose

The authors recommend the following routine nursing orders (1) High

caloric and high vitamin breakfast and supper, (2) no visitors during treatment. The room must be darkened and quiet; (3) sodium amytal gr $1\frac{1}{2}$ to 3 (97 to 195 mg) by mouth after breakfast The dose should be reduced after the first few days, (4) vaccine intravenously at 8 30 A. M; (5) hot water bottles and blankets, loosely applied, (6) codeine gr ½ to 1 (32 to 65 mg) subcutaneously 15 minutes after the vaccine has been given, (7) limit fluids during treatment to cracked ice, sips of plain water, carbonated water or lemonade, (8) record temperatures carefully, every half hour to 103° F. (394° C) ascending, every quarter hour from 103° F (394° C) ascending and descending, each half hour descending below 103° F (394°), each hour descending below 102° F (39° C) until normal for two hours, (9) when the temperature has dropped below 104° F (40° C) the blankets should be removed and fluids given freely

The vaccine treatment is given daily until all signs of chorea have disappeared Using this method of treatment on 50 choreic children, 92 per cent were cured, and ten per cent had a total of six recurrences one to three years following treatment The average length of hospitalization was 29 days and the average number of treatments were 86 Patients with an active carditis but with good cardiac function were included. The only contraindications to this therapy were concomitant conditions so severe as not to permit a patient to stand the strain of a temperature without danger, such as severe anemia, extreme malnutrition, cardiac decompensation, etc There were no complications or death

C A Neymann, M L Blatt, and S L Osmorne² employed *fever therapy* induced by means of electromagnetic induction. For purposes of heat insula-

tion the patient is placed in a treatment bag similar to an outdoor sleeping bag The cable carrying the current is formed into a pancake coil and rests on the patient's chest and abdomen, or it is placed under the patient's back, shaped as an elongated loop extending from the shoulder blades to the middle of the calf With either method, the cable carrying the current is placed outside the bag About 21,2 inches of heat-insulating, nonelectrolytic material such as blankets, cloth, wool or cotton, must be placed between the cable and the patient The temperature is raised as rapidly as possible to 103° F (394° C) after which the current is turned off and the temperature usually coasts a degree or a degree and a half higher This is maintained for a maximum of eight hours

The patient is not permitted breakfast He 15 given a before the treatment cleansing enema before being placed in the bag. During treatment, fruit juices with lactose added, water, and in case of a complaint of hunger, milk may be All liquids should have enough salt added to form a saline solution of 06 per cent Convulsions, a decrease of the respiratory rate to less than 12 per minute, cyanosis, or an increase of the heart rate to 160 or more are indications for immediate cessation of treatment. While an active carditis is not a contraindication to the treatment, complaints of precordial pain and dyspnea by the patient are indications for termination of the treatment

Twenty-five cases were successfully treated. The number of treatments ranged from two for mild cases to nine and ten for severe cases. The treatments were given bi-weekly. The average number of treatments were four and the average length of hospitalization was 16 days. There were three recurrences

H. Lowenburg and S Nemser³ induced hyperpyrexia by means of hydrotherapy in the treatment of chorea The patient is placed in a bath tub filled with water of 80° F. to 95° F. (267 to 35° C) depending upon the patient's comfort Gradually the temperature of the water is raised to 120° F (49° C) by allowing a small stream of hot water to run in the tub The patient remains in the bath at this temperature for at least two hours and if possible for three hours The temperature is taken by mouth if possible every 15 minutes or by rectum with the patient kneeling with the buttocks above the water line The patient's temperature should reach 103° F to 104° F (394 to 40° C) or higher at the end of 20 or 30 minutes and should remain at this level throughout the duration of the bath Fluids at ordinary room temperature may be given during the bath and cool cloths are wrapped around the head until the patient becomes accustomed to the warmth Baths are best given on an empty stomach Complaints of nausea, weakness, or cyanosis are indications for immediate removal from the bath At first, the baths are given daily, then the intervals are gradually lengthened until about a dozen or more have been given. The authors treated three cases of chorea obtaining complete relief of symptoms in two cases and partial relief in the remaining case

V Gillot and R Dendale⁴ used fever therapy induced by malaria in the treatment of chorea. Five cc of blood were taken from a malarial patient during the period of the chill and given subcutaneously. The benign tertian form of the Plasmodium vivax was used. About ten paroxysms were permitted before the malaria was terminated by from one to three injections of 0.50 Gm of quinine Fevers up to 103.3° F (39.6° C) were

obtained Five cases were treated and good results obtained in all cases.

E. Glanzmann and S. Shaffer⁵ treated 22 cases of chorea minor with nirvanol (phenylethylhydantoin) The dosage was determined by the needs of the individual case, mild cases were given 015 Gm once a day, more severe cases 0 15 Gm twice a day and the most severe cases 015 Gm three times a day The drug was continued for 7 to 14 days, and was discontinued at the appearance of nirvanol sickness If no nirvanol reaction occurred, the drug was discontinued after 12 to 14 days The nirvanol reaction usually appeared after an incubation period of about ten days and was characterized by a fever of 1033° F to 104° F (396° C to 40° C), which lasted three to four days or longer and descended by lysis Headache, nausea and vomiting were present A skin rash morbilliform or scarlatiniform in type was present. There may be a decreased leukocyte count in the blood with an increase in monocytes and eosinophils and a decrease in the polymorphonuclear cells While the authors obtained good results in all their cases, cases treated with nirvanol have been known to develop delirium, somnolence, stupor, convulsions, nephritis, agranulocytosis, hemorrhagic cystitis, and in some instances The authors attributed the absence of complications in their cases to the small doses of the drug that were administered and to frequent and careful examination of the blood

J J Jungerhans and J J C P A Roovers' report the successful treatment of five cases of chorea by the *intra-muscular injection of evipal sodium*. The drug was administered in doses ranging from 2 cc to 5 cc given daily or every other day, the frequency and dose depending upon the severity of the symptoms and their response to therapy

Two weeks' treatment usually sufficed to produce cessation of movements

Leslie Cole⁷ reports the successful treatment of a severe case of chorea gravis with avertin. The patient, a child of 11 years, had violent movements involving the entire body, extremities, and face The movements of the face, throat and mouth were so severe as to make speaking, eating and drinking impossible During the first 48 hours in the hospital, in spite of a quiet, darkened room, subcutaneous luminal and hyoscine and bromides per rectum, the movements be-Death from excame more violent haustion seemed likely Avertin, 25 cc (01 Gm per kilogram body weight) was given rectally under chloroform anesthesia The movements were completely controlled and the patient was asleep in 15 minutes The symptoms were controlled for four hours after which they gradually returned to their former violence Treatment with avertin was therefore continued, the dosage being regulated by the severity of the returning movements Each dose was continued at 25 cc, the frequency per 24-hour periods being increased to five doses and then gradually being reduced The avertin treatment was continued for 21 days, the patient beginning to improve on the seventh day and having complete cessation of symptoms by the sixth week Nasal feeding was used for the first ten days. The author points out that it is not yet known what danger, if any, exists in giving repeated closes of avertin Hence it should be used with caution and care when other methods have failed The results with this case suggest that avertin may be the sedative of choice in cases of prolonged cerebral irritation which endanger life from exhaustion In conditions like severe tetanus, status epilepticus, Jacksonian epilepsy, chorea gravis and prolonged convulsions in

meningitis, when milder sedatives fail, avertin used with discretion is probably less dangerous than uncontrolled cerebral irritation on the one hand and the intermittent use of inhalation anesthetics on the other

G E. G Pearson⁸ employed calciumaspirin therapy in the treatment of chorea This was based on the principle advanced by Mutch that chorea was related to a low level of calcium in the spinal fluid, and that recovery was related to an increase of the spinal fluid calcium to normal Twenty-three cases were investigated Calcium gluconate gr xv (097 Gm) and Aspirin gr x (065 Gm) were given every four hours. and patients were kept on this treatment until the chorea subsided, usually for a period of from two to four weeks. The children were kept at rest and in addition were given cod-liver oil and an iron tonic

It was not shown that the chorea was associated with a low level of calcium

in the spinal fluid. While the author believes the treatment materially shortened the duration of the chorea, she points out that this treatment is purely symptomatic. The calcium acts probably as a nerve sedative and the salicylates have a beneficial effect upon the rheumatic infection. The good effects are not related to an increase of the spinal fluid calcium.

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CRANIAL TRAUMA

By Ell Marcovitz, MD

Each year sees new articles on the treatment of cramal trauma, most of which are restatements of old principles. In probably no other group of cases is there so much contradiction concerning what constitutes proper treatment. All this contradiction serves merely to emphasize the one important point in the treatment of cramal trauma which is usually forgotten that the treatment of this problem after the period of shock is over, is an individual problem.

Treatment—The treatment of cerebral trauma is still controversial Chalmers H Moore¹ discusses the pathophysiology and treatment on the basis of 1056 cases He states that a severe blow

to the head produces a dilatation of the arterial side of the capillary loop, causing a sudden rise in hydrostatic pressure and a leakage of serum into the perivascular The consequent changes in osmotic relationship between the perivascular fluid and the blood in the capillary loop lead to further seepage into these spaces The venous capillaries become compressed, causing back pressure in the entire capillary tree, with consequent anoxemia and possibly multiple petechial hemorrhages The medullary centers respond to the anoxemia by producing a rise in the systemic blood pressure and a slowing of the pulse rate, which re-establishes the cerebral circulation until there is a repetition of the cycle. If the cycle is not broken by a reduction of the intracranial pressure, there results complete exhaustion of the centers and death. Cellular destruction due to anoxemia adds to the increased intracranial pressure and may be responsible for permanent post-traumatic difficulties, such as headaches, convulsive seizures and so-called post-traumatic neuroses. Another factor contributing to increased intracranial pressure, is the mechanical blockage of the absorption of cerebrospinal fluid by extravasated red blood cells blocking the subarachnoid villi

The author considers the fundamental group of cerebral injuries to be congestion and edema, contusion and laceration Congestion and edema constitute about 25 per cent of the cases in his series, and are characterized by primary loss of consciousness followed by headache on return of consciousness. There may also be disturbances of memory, and even convulsions and motor weakness. The cerebrospinal fluid does not contain red blood cells, and the pressure is only moderately increased.

Contusion and laceration constitute slightly more than 50 per cent of the author's cases, and are characterized by an exaggeration of the signs seen in congestion and edema, ϵg , deeper coma and increased restlessness, plus a bloody spinal fluid under greatly increased pressure. The amount of blood in the fluid is significant of the degree of damage and influences the prognosis

The important objectives of treatment are the management of shock and the reduction of increased intracranial pressure. No disturbing procedures should be undertaken until the period of actual or potential shock is over. On admission the patient should be wrapped in warm blankets and his temperature, pulse and blood pressure taken every 15 minutes.

Fifty cc of 50 per cent dextrose are given to combat shock if the temperature is subnormal. No detailed repair of scalp lacerations is attempted at this time, but a sterile finger is introduced into the wound to determine the presence of a skull fracture, and a sterile dressing is then applied If there has been appreciable loss of blood, from 250 to 500 cc of physiologic sodium chloride solution is given Extreme restlessness is controlled by the hypodermic injection of phenobarbital sodium. Morphine, or its derivatives, is contraindicated. Solution of posterior pituitary extract and ephedrine sulfate are permissible as stimulants.

The author emphasizes the importance of the patient's position in bed during the entire period of unconsciousness, and recommends the lateral prone posture with the head of the bed at least 12 inches lower than the foot. This aids drainage of bronchial mucus which otherwise may be inspirated, producing cvanosis and adding to the intracranial pressure, and which also may become the starting point of a pulmonary infection

When the temperature reaches 98° F (366° C), neurologic examination may be done, paying particular attention to the depth of stupor, the state of the pupils, the cranial nerves, the muscle tone and the reflexes. The type and rate of respiration is of much prognostic value. Unless middle meningeal hemorphage is suspected, x-ray examination should be delayed until the patient can co-operate fully.

Lumbar puncture should be done to determine the degree of intracranial pressure, by manometric reading, and to ascertain the presence or absence of blood. If the pressure is normal or only slightly elevated, nothing further is indicated unless the clinical picture warrants it. In the presence of an ele-

vated pressure, enough fluid is withdrawn to reduce it to normal. If the fluid contains blood, as much fluid as possible is withdrawn

The author discusses methods of reducing increased intracranial pressure, and recommends *repeated spinal drainage* rather than dehydration, especially in the presence of a bloody spinal fluid Drainage should be repeated at intervals of 8, 12, or 24 hours, depending on the richness of the mixture of blood, until the fluid is clear. If, after a sufficient time has elapsed, signs of improvement do not appear, one is justified in presuming that more serious damage is present, such as subdural or extradural bleeding. Then subtemporal burn openings can be made under local anesthesia.

On the basis of clinical experience with 25 patients with acute cerebral trauma, E. V. Hahn, F. B. Ramsey, and K. G. Kohlstaedt² recommend the use of intravenous injections of *sucrose*

(the usual dosage is 100 cc of 50 per cent solution) instead of dextrose in the osmotic treatment of increased intracranial pressure. Many investigators have reported that following the injection of dextrose solution there occurs an initial fall in intracranial pressure which is succeeded by a rise to a level beyond the original pressure. If sucrose is used, however, there occurs a fall which is sustained, and which after seven to eight hours is succeeded by a final pressure usually lower than the original level.

The authors recommend spinal puncture with pressure readings before the institution of osmotic therapy. They also warn against excessive dehydration, and recommend blood nitrogen studies as a guide

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ENCEPHALITIS

By HINRY A DAVIDSON, M D

The problem of encephalitis is still very much unsettled, and no really new light has been shed on it in the past Much of the confusion is due of course to the fact that included in the category of encephalitis is a large number of encephalitides such as lethargic encephalitis (Economo), Encephalitis-B (St Louis and Japan encephalitis), dissemmated encephalomyelitis, perivenous encephalomyelitis following some of the exanthemata, metastatic encephalitis, polioencephalitis, and various other forms Some of these are due to viruses Of the virus forms of encephalitis, the etiologic agent has been carefully worked out for B-encephalitis of the St Louis type The cause of lethargic encephalitis is still obscure. So too is the cause of disseminated encephalomyelitis and the encephalomyelitides following measles, smallpox, mumps, and chicken pox

Acute Encephalitis

Recording one case of lethargic encephalitis associated with infection of the hand and three of encephalomyelitis secondary to focal infection, S. Heringa¹ suggests that focal infection may reactivate a pre-existing but latent neurotropic virus. He warns against surgical tampering with the teeth in the presence of neurotropic infections. Infection of the cornea was followed by a peculiar

type of acute encephalitis in a case reported by H Hoff and O Poetzel² who find that this infection follows the socalled "trigeminal track." Their case of "track encephalitis," as they designate it, followed herpes in the cornea The virus was transmitted to rabbits, and its identity An unusual form thus established of acute encephalitis beginning with a hemiplegia with crural predominance is presented by M Loeper, A Lemaire, L Roy and Mme Loewe-Lyon 3 The illness began with weakness of the legs Signs of meningitis developed, and a spastic paralysis of Parkinson-like character appeared on one side Death ensued following the development of signs of bulbar paralysis

The health menace presented by painted toys and furniture is stressed by S S Blackman 4 He cites cases of lead encephalitis in 22 children, all of whom had nibbled on painted cribs or painted toys Lesions, which were found throughout the cerebral and cerebellar hemispheres, were those of serous inflammation Thrombosis and necrosis of capillaries were noted, with abundant exudate formation and tissue damage. In many areas, Blackman found foci of gray and white matter diffusely saturated with exudate and made up of damaged glial cells and necrotic neurones The clinical symptoms included convulsions, spastic paralysis and mental retardation

Encephalitis and the Acute Exanthemata

In an investigation of encephalitis associated with vaccination, variola and measles K H Finley finds the chief changes in the perivascular tissues. Progressive glial reaction and demyelinization were noted along the course of the veins. The site of these lesions was dependent on venous distribution in both the brain and spinal cord. In the latter,

Finley found a subpial reaction which was morphologically related to the perivenous reactions. The significance of venous lesions is also stressed by T J. Putnam⁶ who suggests that the primary pathologic feature of encephalomyelitis and of multiple sclerosis might be an abnormal instability of the blood plasma This, he indicates, would allow the blood in the venules of the brain and cord to clot when acted on by certain endogenous or exogenous toxic factors.

While measles and cow-pox are the commonest exanthemata associated with encephalitis, the complication may occasionally develop in the course of German measles Only 17 such instances had been reported prior to 1937, but C F Read adds an eighteenth case His patient, a young adult, developed vertigo, dysarthria, and incoordination two days after the onset of a rosy-colored eruption on the chest which, occurring during an epidemic of rubella, was identified as German measles A few days later, the symptoms included nystagmus, diplopia. stiff neck, and twitchings of the extrem-Treatment consisted of spinal tap, proctoclysis and intravenous administration of dextrose and the use of sedatives On the tenth day after the onset of the encephalitic symptoms, he was well enough to return home. In view of the frequency of German measles, this complication should be kept in mind

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EPILEPSY AND THE CONVULSIVE STATE

By HENRY A DAVIDSON, M D

Incidence—Of the half million persons in the United States subject to convulsive attacks, all but ten per cent are in the community at large, according to figures prepared by W G Lennox ¹ Only a very small proportion of these (fewer than five per cent) are hopelessly deteriorated From 20 to 40 per cent of the epileptics are only moderately deteriorated and are able to feed and clothe themselves and to do simple tasks. The remaining group, comprising about 60 to 80 per cent of all epileptics (representing from 300,000 to 400,000 persons) are substantially of normal mentality.

Mortality—On the basis of a study of the inmates of New York institutions, B Malzberg² concludes that the crude death rate among patients with epileptic psychoses is seven times as high as the general death rate in the population at large. In this group, the commonest assigned cause of death is the epilepsy itself, with heart disease, tuberculosis and pneumonia as the next most important causes. The death rate from tuberculosis is higher among patients with epileptic psychoses than among schizophrenics.

Heredity — Studies which seek to evaluate the hereditary factor in epilepsy have usually been made in colonies and institutions, and have therefore reflected the status of deteriorated patients. H. A. Paskind and M. Brown, however, analyzed the records of 331 nondeteriorated, well-adjusted patients and found evidence of a "hereditary neuropathic taint" in 58 per cent of them. Of relatives exhibiting this "taint," the commonest abnormality was migraine (38 per cent), while the next most frequent finding was "nervousness" (32 per cent). Epilepsy itself occurred in only 14 per cent of the

family records In a comparable study of detriorated epileptics, the proportion of "hereditary neuropathic taint" was 81 per cent. This suggests that the epileptic who is destined to deteriorate carries a heavier hereditary burden than the essentially nondeteriorating type.

A structural basis for the higher proportion of bad familial records in deteriorated patients, is suggested by another study made by H. Paskind and M Brown,⁴ who found physical stigmata more common in the deteriorated group This speaks for a higher proportion of cerebral developmental anomalies in these patients, and perhaps thus accounts for the deterioration

Onset-J L Fetterman and V R Hall⁵ examined records in 160 cases of epilepsy and found that the onset was violent or sudden in about three-quarters ot the patients This is contrasted with the "gradual" onset types in which, prior to the first real convulsion, the patient complained of a variety of odd, peculiar and vaguely localized sensations Seventy-eight per cent of those in the "violent" group had their first paroxysm prior to the age of 21, while 85 per cent in the "gradual" group reported their first seizure before that age A family history of epilepsy was present in 27 per cent of the violent and in only 14 per cent of the gradual types No correlation was found between the type of onset and the response to treatment, intelligence, or the ultimate outcome

Precipitants of Attacks—Camphor apparently precipitated an epileptic seizure in three patients reported by P Pagniez, A Plichet and A Varay ⁶ These authors were able to elicit convulsions and increase acoustic and tactile irritability by giving camphor salts to experi-

mental animals They warn against the indiscriminate use of camphor bromide, and suggest that before using this drug. the physician should test the patient's susceptibility Music was responsible for precipitating an attack in eleven cases reported by M Critchley 7 In most of these patients, no seizure occurred unless the musical stimulus was present A method of experimentally provoking attacks without producing pain or apprehension and without impairing the organic intactness of the animal, was suggested by F A Fender 8 The skull was opened and an electrode anchored near the posterior sigmoid gyrus After the wound was closed, the animal was permitted to move about freely for three days Then, with an indifferent electrode under the temporalis muscle, the animal was placed in a room bathed in a fluctuating magnetic field. An alternating current with a 60-cycle frequency following a sine wave was employed resultant attacks minicked idiopathic epilepsy in all its clinical features

Carbohydrate Metabolism in Epilepsy

That convulsive disorders are associated with hypoglycemia has long been known Further evidence that such a relationship exists is afforded by the recent reports of the usefulness of insulin in dementia precox, for G Kraus, F Vandermeulin and 1 M Rombouts9 cite clinical findings suggesting a biochemical antagonism between dementia precox and In a group of schizophrenics, they secured favorable results by provoking epileptic-like seizures by injecting camphor A complete biochemical explanation for the negative association between hypomsulinism and epilepsy is offered by E Powell 10 Lactic acid, the only fuel required by the brain, is the product of glucose metabolism When glucose is reduced, the fuel of the brain is in peril, and with the diminution in the supply of the cerebral nutrient, unconsciousness ensues To secure the essential dextrose, the body produces the convulsion, which through the resultant excessive muscle activity, elaborates large quantities of lactic acid out of which a supplementary supply of dextrose may be manufactured Powell's clinical observations indicate that epileptics generally exhibit a hypoglycemia, a finding which accords with this hypothesis He suggests that pancreatic (insular) hyperactivity is the basic disturbance in epilepsy. This thesis is quite at variance with the findings of L J Pollock and B Boshes, 11 who found fasting levels for dextrose to be within normal limits among 90 epileptics Their sugar tolerance was normal, and when hypoglycemia was provoked, no convulsions were precipitated

Physico-Chemical Findings in Epilepsy

The morganic soluble phosphorus content of the blood rises during an epileptic seizure To determine whether this was due to the phospholipids of the central nervous system, A Weil and E Liebert12 first provoked convulsions in rabbits by injecting thujone The usual rise in blood However, when phosphorus occurred the musculature was immobilized with curare, the same procedure affected no alteration in phosphorus content, thus suggesting that the source of the high phosphorus value during a paroxysm is the contraction of the muscles which characterizes the seizure In general, epileptics had a low volume of circulating blood, according to the studies of I Finkelman and D Haffron,1; who found a blood volume of from 2300 to 2500 cc per square meter of body surface This compares with normal figures of from

3000 to 3400 cc Reviewing 61 studies of the physicochemical factors in epilepsy, M. Brown and H. A Paskind¹⁴ found little of significance. There was some evidence that the underlying mechanism of the paroxysm depended on changes in the colloidal character of the nerve cell membrane in response to a primary humeral disturbance The seizures were accompanied by increased electrical activity within the cerebrum, and the clonic movements appeared to be synchronous with waves of electrical activity in the cortex But there was no evidence of changes in intracranial pressure and no consistent increase or decrease in the permeability of the hematoencephalic barrier

Water Metabolism in Epilepsy

The validity of the hydration theory of epilepsy is doubted by T T Stone and H Chor 15 They submitted 18 epileptics to a period of hydration when fluid was forced by mouth and pitressin given to assist in maintaining water re-The incidence of convulsions was not increased during this period Fach patient was then subjected to "dehydration" by denying all beverage intake and limiting total fluid intake to a liter a day. There was no reduction in the number of seizures during this period. Metabolic studies indicated that there was no real tissue hydration or dehydration in spite of the heroic clinical measures

Neuro-Physiologic Mechanism in Epilepsy

Ordinarily the autonomic nervous system maintains balance (homeostasis) between (a) the forces acting on the central nervous system, and (b) the forces acting within it. The sympathetic division favors mobilization of the energy reserves of the body and increased activity of the

cerebrospinal nervous system, while the parasympathetic division diminishes cerebrospinal activity and favors anabolic restitution of energy P I Yakovlev16 calls attention to the parallelism between sympathetic activity (mobilizing energy) and epileptic paroxysms on the one hand, and between parasympathetic activity (anabolic restitution) and the recovery from a seizure on the other He suggests that during the attack, the sympathetic division, and the posterior hypothalamic complex, including the mamillary body, are overstimulated while the parasympathetics and the anterior hypothalamic structures, including the tuber cinereum. are inhibited During the period of recovery from the paroxysm, these would be reversed On this theory, the hypothalamus and its adjacent structures would represent the head ganglion of the autonomic nervous system The anterior hypothalamic complex is connected with the craniosacral division and the posterior complex with the thoracolumbar division of the autonomic system The whole seizure is thus thought of as a disturbance of one central reflex mechanism

Encephalographic Diagnosis

Encephalography is recommended by F. Laubenthal¹⁷ as a safe and useful diagnostic method in epilepsy. In the hereditary ("idiopathic") cases, he finds chargements and dilatations of the ventricles, while in the Jacksonian and other exogenous cases he notes more specific or more extensive damage, such as local subarachnoid fluid lakes, ventricular displacement or hydrocephalic dilatation.

Convulsions in Childhood

Warning that convulsions in childhood may establish an "epileptic potentiality," R G Armour¹⁸ urges the affirmative, intensive treatment of these conditions

When gastrointestinal conditions provoke a seizure, the practitioner should not treat the stomach or the intestinal complaint and dismiss the convulsion with the thought that the child will "grow out of it" Instead, the attack should be studied and specifically treated Similar advice is given with respect to convulsions associated with sunstroke

Jacksonian Epilepsy

In an analysis of 82 cases of Jacksonian epilepsy, A Sozon-Yaroshevich¹⁹ found 16 per cent due to tumor, five per cent to echinococcus cyst, 35 per cent due to inflammatory or degenerative diseases, and the remaining 44 per cent due to head injury Between the primary disease (or trauma) and the first convulsion, the average elapsed time was 31/2 vears Cortical scars and pial hyperemia were found in only half the cases, while in every instance, pathologic study disclosed pial edema, new vessel formation, and serous arachnoiditis The fundamental change seems to be obliteration of the subarachnoid space with changes in the blood vessels and secondary alterations in blood and spinal fluid circulation Cortical scars can be extensively and successfully removed in these cases, in the opinion of J. T. Gilbert,20 who recommends identification of the involved cortical area by faradization with radical excision of the affected tissue. The resulting paralysis is only temporary Calbert believes, however, that surgical intervention is of greatest benefit in convulsive disorders when the seizures are due to brain tumor

Convulsive Disorders and Anesthesia

When convulsions occur while the patient is in a state of induced general S Lundy and E anesthesia. I Tuohy²¹ urge the prompt administra-

tion of anticonvulsant medication Soluble barbiturates may be given intravenously, and an operating room should be equipped with such drugs Since this complication is more likely to occur when the patient is young and septic, especial care should be taken with general anesthesia in these cases It is well to consider the use of local anesthesia under these circumstances These findings and suggestions are in accord with the observations of R V Payne²² who finds four factors responsible for the seizures. These are a warm operating room, a young patient, deep anesthesia, and the presence of sepsis When convulsions occur on the operating table, the anesthetic should be discontinued, a clear airway established, the head raised, carbon dioxide administered, and the lungs insufflated Large doses of chloral hydrate or potassium bromide should be given rectally in these cases

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FEEBLEMINDEDNESS

By Robert A Matthews, BS, MD

A study conducted in Germany dealing with the importance of heredity in feeblemindedness seemed to indicate that the recent trend away from the belief that heredity is of great importance as an etiological factor in mental deficiency is not justified, since over 75 per cent of the cases studied were demonstrated to have an hereditary background Kleindienst studied the age of parents and order of birth in connection with mental and physical defects of offspring and discovered that the fifth child is more often involved as regards physical detects, the mother generally being more than 30 years of age, although the first born was often affected and the defect frequently thought to be related to birth injuries. Manne analyzed the effect of inbreeding for several generations between members of a defective family which revealed conditions that resulted in many instances in early death, illegitimacy, drunkedness, murder, cancer, mental disease and poverty

Etiology-Iron somatic and psychologic examination of 375 premature children ranging in age from 7 to 15 years, Brander¹ found that in the group with graver traces of earlier rickets there was greater frequency of feeblemindedness, cases bordering on feeblemindedness and ordinary stupidity, while the number of normal and talented children was correspondingly less Since the defects in intelligence were of relatively mild degree, he concludes that rickets can hardly be of practical significance in the etiology of oligophrenia There was no evidence for or against rickets as leading to lasting mental deficiency of milder degree, but both rickets and defective mental development might have the same cause, as, for example, premature birth It seems to the author fairly certain that mental deficiency in itself 15 something which promotes the origin of rickets

Therapy—In discussing the mental growth in epileptic children, Kugelmass, Poull, and Roudnick2 state that whatever the intellectual endowment of an epileptic child, his mental growth is retarded more often than exhilarated One hundred twenty-nine epileptic children were studied along clinical and psychological lines. The children were classified as primary if idiopathic epilepsy was the sole disturbance, and as secondary if, besides epilepsy, there was a constant cerebrogenic factor superimposed on the mental status. The children were considered improved if either or both the number and intensity of the seizures diminished, and unimproved if either or both of these conditions did not ensue The mental tests involve a variety of appropriate scales, an average of which constitute a final rating for each child It was found that the institutionalized group of epileptic children is retarded mentally but within the range of the hospitalized unselected children The private practice group of epileptic children show a mental rating significantly higher in the improved than in the unimproved patients. The large number of mentally retarded epileptics observed in the institutionalized group is statistically balanced by a greater number of cases above average intelligence in the private practice group. The authors believe that mental deterioration is prevented by treatment in both institutionalized and private practice groups.

In an article dealing with acetarsol in the treatment of late congenital syphilis among mental defectives Paddel3 concludes that acetarsol is a drug with a powerful salvarsan-like action on cases of congenital syphilis It has the added advantage of oral administration, rendering possible the treatment of large numbers of cases with the minimum of apparatus and great saving in time It will be found very useful in those large mental hospitals and mental defective colonies where the patients are under constant care and supervision. If the scheme of dosage as given in this paper is adhered to there will be little likelihood of serious toxic reactions resulting close relationship of acetarsol to tryparsamide, and the fact that many abnormal cerebrospinal fluids were improved and two cases of juvenile general paralysis benefited, suggests the desirability of further research along these lines

Perhaps treatment aided by other antisyphilitic drugs may be found more effective, but there is little doubt that acetarsol is entitled to a place in the modern treatment of congenital syphilis

At a meeting of the Bucharest Pediatric Society, Dr. Calimanescu⁴ stated that, in the treatment of backward or mentally deficient children, *medical gymnastics* is useful as a prelude to *physical education*. The treatment must of course be strictly individualized. Its effect is to develop the latent potentiality

of the brain cells. Increase in muscular power goes hand in hand with progress of mental development and improvement in the child's sensory condition. The chief aims of medical gymnastics in cases of mentally deficient children are to aid in developing the efficiency of the motor, sensory and psychic elements of the cerebrospinal system, the sympathetic system, and generally to improve the con-The exercises are passive stitution manipulations, mechanical shaking and strong vibration applied over the brain and spinal cord, and local nerve friction Auditory and visual stimulation is afforded by telling the child to perform or to imitate movements. Active and passive, or resisted, movement of the joints may be associated with other forms of treatment

Heredity-McPherson⁵ in a consideration of the heredity of mental deficiency points out that a superintendent of a training school for mental defectives in Massachusetts not long ago reported that only 12%, per cent of the patients in his institution could be considered cases of familial defect. This statement was found to be greatly at variance with the author's experience in an institution at Belchertown, Massachusetts, since a preliminary survey of the population of the institution indicated that a least 50 per cent of the admissions may be readily classed as familial However, it was pointed out that this particular institution is recognized as serving a district comprising the western half of Massichusetts in which there is a great deal of deficiency obviously transmitted from one generation to another, and which his resulted in so much incompetency and dependency that whole families, or large parts of families, have been committed to the institution to relieve the communities of further burdens. It would appear that in rural western Massachusetts.

where the march of industry has called active workers away from small hamlets and into large cities, a great many of the less competent have been left behind. The author cites a number of family groups which epitomized this problem

The Mental Deficiency Committee of the Royal Medico-Psychological Association made an inquiry into the incidency of "neuropathic" conditions in the relatives of normal persons6 in order to compare the percentage of these conditions found in the ancestors of normal people with those found in the ancestors of the feebleninded population questionnaire asked for information about the following relatives siblings, parents, uncles and aunts, nephews and meces, and grandparents The presence of the following abnormalities were recorded fits, paralysis, deaf and dumb, blind, insane, weak-minded, rather peculiar, alcoholic, tubercular, mental condition normal, mental condition not known

Four hundred fitteen forms were returned and examined. It was found that 57 per cent of normal informants gave a positive family history. Excluding the mimor conditions, 23 per cent of the intormants gave a history of some largely neurological or psychiatric abnormality in the family. Although it was recognized that certain errors were hable to give too low a figure and the committee agreed that the figures may be accepted as lower limits to the true figures.

Pathology — A Meyer and L C Cook? in an article entitled "Diffuse White Matter Gliosis in Mental Defectives" make a preliminary report of investigations into the pathology of mental deficiency Twenty-two cases comprising seven low-grade defectives showing gross neurological lesions, chiefly of extrapyramidal character, six microceph-

alics with spastic diplegia and severe mental defect, two able-bodied microcephalics without gross neurological signs, one simple able-bodied idiot and six mongols, were studied A particular finding occurred with surprising constancy, i e, a proliferation of the fibrous glia particularly pronounced within the cerebral and also the cerebellar white matter In many of the cases the cortical changes were slight compared with the intense lesions of the white matter In none of them was demyelinization a well-marked feature nor did its severity approach that of glial proliferation The gliosis was either diffused or patchy, and was often markedly perivascular The pathogenesis of the gliosis is at present obscure but in some of the cases there was some evidence suggesting that a vascular factor or some other type of defective tissue oxygenation might be the immediate cause of the change in the high incidence of the lesions within the white matter This was pointed out in reference to the view expressed by Bodechtel that it is the white matter which is particularly susceptible to oxygen deprivation in the developing brain in contrast to the adult brain in which the cortex is more vulnerable

Delinquency and Intelligence

The mental ability of delinquent boys has been studied by H. A. Lane and P. A. Witty 5. The authors point out that in 1914 Goddard proclaimed that at least 50 per cent of all criminals are mentally defective. Scrutiny of the methods used in the early studies shows that generalizations of this nature were premature and hyperbolic. The results of mental tests administered to about 700 delinquent children in the St. Charles (III.) School for Boys are analyzed. The intelligence of more than 80 per cent of these delinquent boys was below the

average for unselected children studied by Terman, and ten per cent were feebleminded Recidivists are frequently alleged to be duller than children who are serving a first term in a state school This was not found to be the case in this study. The group of boys who committed burglary included the largest number of bright children, while the groups of "truant and runaway" boys contained no bright child. The intelligence quotient appears to be unrelated to the extent or the seriousness of the delinquent behavior Lane and Witty believe, however, that their search for factors associated with the intelligence of delinquent children has been rather unsuccessful They cannot point to a single item which seems significantly related to the results of the intelligence tests However, they demonstrated the falsity of many assertions regarding the role which intelligence assumes in the behavior and lives of delinquent children.

Mongolism

Bleyer¹⁰ made a study of 2822 cases of Mongolism through the questionnaire method with the view of determining the role of advancing maternal age in the production of this condition. His conclusions coincide with those of Jenkins and Penrose that the role of advanced maternal age is undeniable in Mongolism. He found that the peak of maternal age in the general population in this country in 1934 was 24. The peak age of the Mongoloid producing mother was

41 The incidence of Mongolism increases steadily through the child bearing period, being lowest at the beginning, and highest at the end, the likelihood of producing a Mongoloid imbecile increasing in direct proportion to the number of menstrual cycles through which the woman has passed No satisfactory evidence of the following factors in relation to the etiology of Mongolism could be found: Advanced paternal age, immaturity of either parent, primogeniture, ultimogeniture, birth rank, broad difference in the age of parents, prolonged interval preceding the birth of the Mongoloid; low fertility, reproductive exhaustion of either parent.

It is considered probable that the apparent relation of any of these may be explained through admixture of advanced maternal age

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MANIC-DEPRESSIVE PSYCHOSIS

By JAMES A FLAHERTY, M D

Alterations in the Fundamental Concept — The nosological grouping, manic-depressive psychosis, has been used in a very decisive way, carrying with

It the inference of a definite prognosis Recovery is assumed and the question is only one of duration of the episode, and of subsequent attacks. The clinician

is confident of a benign, even if repetitive course. The essential fallacy of this conception is stressed by Aubrey Lewis ¹. He feels it best to think of a wide range of affective psychoses, with an extreme group, in which constitutional factors are vastly more important than environmental ones, and milder affective states, readily responsive to situational factors, mostly with depression and anxiety, and with a general drift toward chronicity

Leslie B Homan² in a seven-year follow-up of a series of 144 cases, comments that only 11/13th showed elation, and further remarks that he cannot beheve that we are looking at the same illness in all affective disorders. He feels it wise to abandon the classical descriptive categories, since they contribute so little to prognosis and therapeusis Reenforcing this attitude is the discussion by Bertram D Lewin,3 who calls attention to a neurotic type of hypomanic reaction. He differentiates the true hypomanic picture from the neurotic one by the fact that the latter does not make the extensive use of the mechanism of denial employed by the true hypomanic He feels that the neurotic type represses or uses a compulsive-obsessive reaction to deal with unwelcome psychological material. He believes the mechanism of identification is important in both types

Increasingly accepted is the separation of involutional melancholia from the manic-depressive psychoses. Hoch and McCurdy's constitutional and personality conceptions have been widely corroborated, and emphasized most recently by the studies of H. D. Palmer and Steven S. Sherman (Personal communication)

Robert C Hunt and Kenneth E Appel⁴ in a study of reaction types with an almost equal admixture of schizoid and cycloid symptoms, present evidence that these represent a group affording clearer clinical understanding and distinctive

prognosis Of the 30 cases which they collected during the years 1919 to 1929, and have followed to date, a recovery rate of 367 per cent was observed, while 333 per cent were unrecovered, never attaining a remission These authors remark, therefore, that the recovery rate in schizomania, so-called, is roughly twice as great as in schizophrenia (in the absence of insulin therapy), and from 25 to 50 per cent lower than that found in the true manic-depressive psychosis

Heredity-Elliot Slater⁵ presents an illuminating study of 3000 cases (1904-1922) of manic-depressive psychosis studied in Kraepelin's Clinic in Munich Employing careful diagnostic criteria and excluding cases presenting schizophrenic features, he was able to obtain a group of only 72 pure manic-depressive cases A second group of 68 was also studied These, however, were featured by exaggerated hypochondriasis, intense irritability, and/or a basic paranoid personality matrix. He feels that the previous work on the inheritance of manic-depressive psychosis has failed to meet the strict requirements demanded in genetics He concludes that there is no single gene responsible for the condition known as the manic-depressive constitution commenting on the importance of the genotypic milieu, he remarks that any single quality is probably contingent not upon a single gene, but rather on the totality of genes He concludes that even though one gene were responsible for the deviation, the degree to which it would become manifest is governed by a variety of circumstances, genetic, environmental and confusional (exogenous)

Lewis, commenting on genetic prognosis, finds maximum inheritance where both parents exhibit clinical manic-depressive episodes, or where one parent is definitely manic-depressive while the other is melancholic, sanguine or cyclothymic Where one parent is normal and the other manic-depressive, one-third of the siblings show the disorder

Etiology-L J. Karnosh and J. M Hope⁶ in a study of puerperal psychoses and their sequelae, present interesting data on women of cyclothymic disposition who developed an affective psychosis following childbirth The various deliria with affective changes occurring during the lactation period eventuated in subsequent manic-depressive attacks, to which the patients had not before been subject The authors feel that the toxicaffective illnesses induce an organic change, which thereafter expresses itself in the form of a more exaggerated cyclothymic disposition. This organic conception when juxtaposed with that of James Papez⁷ concerning the mechanism of emotion, should encourage illuminating speculation and study

Prognosis—Lewis feels that the outlook for complete recovery is good in an individual with a manic-depressive episode, where a solitary or periodic, but typical affective illness occurred in only one parent. He suggests doubt as to eventual outlook in cases in which eccentric, neurotic or schizophrenic antecedents are predominant. In syntonic individuals with pyknic habitus, who undergo uncomplicated attacks, the return to health is more likely than in individuals in whom schizoid or other psychopathic personality factors enter the picture. He calls attention to the fact that the patient who prepsychotically presents morbid traits 1 c, who is anxious, frictional, suspicious, odd, solitary or obsessional, undergoes no magic alchemy of the personality through an affective explosion, on the other hand, recovery from such an episode may be long drawn out Earl D Bond and F J Braceland8 in a follow-up of 171 manic-depressives

admitted for hospital care in 1927-1928, found 86 of this group recovered. The total of 171 represented 24 per cent of the admissions to the Pennsylvania Hospital in 1927-1928, and contrasted curiously with the figure of 1.5 per cent, or 11 manic-depressives out of 735 total admissions in a comparable period at Burgholzli Anstalt in Switzerland. This is of particular interest from the standpoint of geographic incidence, if the difference in diagnostic criteria is not too broad. Of 8000 cases of manic-depressive psychoses in the New York State hospitals between 1910 and 1919, the Commission statistician, reporting to Dr. Adolph Meyer, states that 50 per cent of first attacks, 25 per cent of second attacks and 10 per cent of third attacks were permanently well

Therapy—Therapeutic approach to manic-depressive psychosis has not been stimulated by the discovery of new methods such as insulin or metrazol therapy in Dementia Praecox H Tomasson⁹ used ephedrine and acetylcholine with some small encouragement from the results Benzedrine has been used with modest success in the mild cyclothymic depressions, and depressed states of which the core is essentially psychoneurotic J Loman, A Meyerson, W Dameshek, and E. Guttmann¹⁰ have made interesting reports on the use of this new sympathonimetic drug in psychiatric practice

T J Hennelly ¹¹ successfully employed prolonged narcosis with *Somnifen*, while H D Palmer and F J Braceland, ¹² reporting on six years' experience with *sodium amytal narcosis*, feel that it is a valuable instrument, the most dramatic use of which is in the acute manic attack. These authors reported a series of 100 treated cases. Of these, 32 were manic episodes, 60 per cent of which had an immediate remission,

while 27.5 per cent showed permanent or temporary ability to maintain a higher level of social adjustment following narcosis treatment E A Strecker, H. D Palmer and F. J Braceland¹³ used synthetic hematoporphyrin hydrochloride in cases of manic-depressive depression, and observed improvement in 36.4 per cent, with moderate improvement in 18.2 per cent

Harold A Palmer, 14 of Woodside Hospital, London, published the most comprehensive review of narcosis therapy in mental disorder yet to appear in the literature. He feels that the useful therapeutic effect of narcosis is related to the narcotic effect upon (a) the cortex, (b) the sub-cortical region, (c) the cortical-sub-cortical balance, (d) the sudden withdrawal of sedatives after their prolonged use (c) the specific barbiturate effect. (f) the tacilitation of psychotherapy during sleep

He enumerates and analyzes the different methods employed, such as that of Klasi. MacLeod, Wolff, Withold and Meerloo He also briefly discusses Cloettal and its use at Zurich. He investigated the recovery rate in manic-depressive psychosis, schizophrenia, anxiety states and alcoholism with narcotherapy. He has also compared the response of the Kretschmerian types of habitus to narcosis finding the pykine type to be most benefited.

He teels that factors bearing on recovery, utilizing this therapeutic instrument, are (a) the duration of the psychotic episode, (b) the age of the patient, (c) the amount of sleep secured and (d)the presence or absence of complications peculiar to the treatment

In addition, he quotes Muller, who has collected to date all the mortality figures since 1925, which is five per cent He discusses the mode of action of narcosis and evaluates its usefulness as a therapeutic method in the psychoses briefly as follows (a) In a mixed series of cases it yields 331/3 per cent recoveries The recoveries occur especially in psychotic episodes which otherwise have a good prognosis (b) These recoveries are due to treatment (c) Since there is a five per cent mortality rate, the risk should be anticipated by scrupulously careful nursing (d) The effect of treatment is due probably to both somatic and psychological factors

The author has collected a most comprehensive hibliography on the subject

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MENINGITIS

By HENRY A. DAVIDSON, M D

Recent advances in the field of meningitis have resulted in the recognition of lymphocytic chorio-meningitis as an entity, the treatment of meningococcus meningitis by means of antitoxin, and the treatment of streptococcus meningitis by sulfanilamide. Chorio-meningitis has been found to result from a virus infection which can be reproduced in white rats The results of treatment of meningococcus meningitis with antitoxin are not yet definitely known, but the outlook is good. The most hopeful aspect of the meningitis problem is the report of scattered cases of streptococcus meningitis which have been cured by the use of sulfanilamide given by mouth, or in some cases intrathecally Any drug which gives a ray of hope in the treatment of this utterly hopeless group of meningitides is worth careful study, and it is hoped that the future will demonstrate the specific value of sulfamilamide in the treatment of streptococcus meningitis

Tuberculous Meningitis

Diagnosis - In an analysis of the records of 14,000 hospitalized children, P Nobecourt and S B Briskas1 found 344 cases of tuberculous meningitis. The disease is very rare in infants under a year old and increases in frequency. reaching its maximum during the fifth year of lite. There is a seasonal fluctuation, tuberculous meningitis being most prevalent during the spring. The duninution in the incidences of tuberculosis generally during the last few decades, has been accompanied by a corresponding reduction in the frequency of tuberculous meningitis For the very early diagnosis of this disorder, M Weichsel and G Herzger2 suggest the determination of the spinal fluid sugar content. This is diminished very early in the disease in several of their cases, the reduction occurred a month prior to the death of the patient. The importance of the bovine organism as a cause of tuberculous meningitis is stressed by E. Lesne, A. Saenz, M. Salembiez, and L. Costil³ who point out that the disease is commoner in areas in which there is a wide use of crude dairy products. They find adults in the immediate surroundings of the affected child who are giving off large numbers of bovine bacilli

Influenzal Meningitis

The mortality rate from influenzal meningitis is about 95 per cent. A case with recovery, however, is recorded by I. Cohn⁴ whose patient developed this disease after a head injury in which the skull was fractured and the brain lacerated. Recovery was complete. The chief therapeutic agent was the lumbar puncture in all, 29 spinal taps were required. Dehydrations, sedatives, and blood transfusions were effective accessory measures.

Meningococcic Sepsis

The diagnostic difficulty presented by a case of meningococcic sepsis is illustrated in a report made by K Kummerling. The symptoms were headache, fever, and skin eruption and the tentative diagnosis was paratyphoid fever. The blood culture revealed diplococci which agglutinated with a meningococcus serum. After treatment—which consisted of the intravenous and intramuscular injection of the serum—the patient rapidly improved and eventually recovered.

Serous (Lymphocytic) Meningitis

Described variously as "benign," "lymphocytic," or "serous" meningitis, an acute meningeal irritation associated with

lymphocytosis and running a short course has been known to the medical literature (M Dummer. for several decades R. A Lyon and F. E Stevenson⁶ review an epidemic of 22 cases occurring in Chicago Headache, voniting abdominal pain, and drowsiness occurred in most of the patients The onset was usually sudden The headache was not so severe as that noticed in septic meningitis, and the vomiting was never projectile Spinal tap usually relieved both of these symptoms Except for stiff neck and positive Kernig or Brudzinski signs, the neurologic examination was negative temperature seldom exceeded 102° F (39° C), and rapidly descended during the first week or two of the illness spinal fluid showed a lymphocytosis and increased globulin content in the typical Except for lumbar puncture, the only treatment was sedative medication Dummer and his colleagues do not believe that the disease is contagious. The differential diagnosis from encephalitis, typhoid fever, poliomyelitis and septic meningitis is essential. The short and benign course, the relative scantiness of the neurologic findings, and the characteristic spinal fluid lymphocytosis should serve to establish the diagnosis. In this series all the patients recovered, and the authors teel justified in characterizing the disorder as a Benign or Aseptic Meningitis

In spite of this designation, however, lymphocytic meningitis may be severe and even tatal. One of the few fatal cases on record, and the first to be subjected to autopsy is reported by H. R. Viets and S. Warren T. Their patient presented the clinical picture above described, but in addition displayed photophobia and blurred optic discs. There was also urinary retention, increased drowsiness, and eventually a convulsion followed by death. Autopsy showed de-

structive changes in the ganglion cells. particularly in the midbrain and menin-Another instance in geal infiltration which lymphocytic meningitis was definitely not benign is recorded by L F. Barker and F R Ford 8 Their patient gave evidence of meningeal irritation, and the spinal fluid contained 450 lymphocytes and 50 polymorphonuclear leukocytes per cmm The specific virus of Rivers and Scott was isolated from the spinal fluid, and the case thus appeared to be a typical example of lymphocytic meningitis However, as the patient developed a paralysis of the lower extremities accompanied by an anesthesia below the level of the fourth thoracic segment. a laminectomy was performed, revealing a chronic obstructive arachnoiditis at that segment The patient remained permanently crippled, although the serologic findings definitely classified her condition as one of "benign" lymphocytic meningitis

The possibility that aseptic meningitis, in some of its forms at least, may be associated with infection of domestic animals is suggested by two recent European reports H Fatzer9 calls attention to the remarkable clinical similarity between lymphocytic meningitis and the disorder identified in Switzerland as "Maladie des Jeunes Porchers"-i e, "Disease of Young Swineherds" It is a meningeal irritation occurring in young people who attend pigs. A similar suggestion is advanced by G Charleux10 who finds the condition among young workers in the dairy areas, especially among cheese makers As the by-products in the making of cheese are fed to pigs, these observations seem to correlate with those of Fatzer It is significant that in the United States, lymphocytic meningitis is more common in children, and since children are more exposed to the virus infections of domestic animals than are adults, the possible relationship between these factors is suggestive.

Complications and Sequelae-An instance of meningococcic meningitis complicated by a blood stream infection with Salmonella Suipestifer is recorded by M. M. Ravitch and J. A. Washington.11 The organism was identified by blood culture and by agglutina-After seven weeks of tion reactions illness the patient recovered The good result is ascribed to the strong antibacterial reaction set up by the meningitis and by the accompanying intraspinal serum treatment. In a six-year period, 28 cases of infection with the suipestifer bacıllus were found in hospital records Almost all the cases were in Negro children

Lazar¹² finds that endoph-NK thalmitis and paresis of the external rectus muscle are the commonest of the complications of meningitis They arise from the fact that infection in the blood stream sometimes reaches the posterior segment through the retinal or choroidal vessels Ocular complications are more common in cases in which the antimeningococcus serum is used intrathecally only. When the intravenous route is the chief avenue of treatment, these complications are less frequent. To diminish ocular complications, W P Eagleton13 suggests that cases in which nystagmus is a symptom require injection of serum directly into the basal cistern If emboli lodge in the eveball, serum may be injected into the anterior chamber or even into the vitreous. When meningococcic meningitis is producing definite elevation of intracranial pressure, surgical relief of this hypertension is justified In an analysis of post-meningitic ocular disorders, P Heath¹⁴ found muscular disturbances more frequently than any other complication. Next in order were endophthalmitis, changes in

the fundi, and pupillary disturbances Most of the permanent changes occurred early in the disease, and many of the ocular complications which appeared late in the course of the illness were only transient Ocular complications are especially common in luetic meningitis, and C. N. Frazier and J W Mu15 report on the analysis of 169 consecutive cases of acute syphilitic meningitis. Because of the basilar site of the involvement, cranial nerve complications were frequent. Implication of the cochlear and vestibular divisions of the eighth nerve occurred in a high proportion of the cases

Treatment—The 1937 literature on the treatment of meningitis has been characterized by large numbers of reports on the use of prontosil and sulfanilamide. While prontosil seems effective only in streptococcic cases. sulfanilamide has been found valuable in the meningococcus form Francis F Schwentker, Sidney Gelman and Perrin H Long16 used the drug in a series of ten consecutive cases of epidemic cerebrospinal meningitis All but one of the patients recovered, a response which compares favorably with that which follows serum therapy Sulfanilamide is paraamino-benzene sulfonamide, and is administered both intraspinally and sub-The solution is made by cutaneously dissolving enough of the drug to make an 08 per cent solution in boiling saline It is given when it has reached a temperature of 986° C (37° C), being allowed to cool to that point after the sulfamilamide has been added. The dosage for intraspinal use is from 1; to 1 ounce (10 to 30 cc) For subcutaneous administration, a dosage represent- $_{\rm ing}$ 31' ounces (100 cc) of the solution for each 40 pounds (18 kg) of body weight, is employed Injections of each are made daily until improvement

15 evident. No untoward effects were noticed

Sulfanilamide was also found effective in the treatment of meningitis due to the beta-hemolytic streptococcus F F Schwentker, F P Clason, W A Morgan, J W Lindsay and P H Long17 report recovery in three out of four cases The solution described above is employed for intraspinal use, supplemented by tablets (one gram each) administered orally For adults, the daily oral dosage is five tablets

The joint use of sulfanilamide and prontosil is recommended by several effective therapy authors as streptococcic meningitis Edward D Anderson18 reports a case in which 5 cc of a 25 per cent solution of prontosil was given intramuscularly twice Prontosil is the disodium salt of 4-sulfamidophenyl-2azo-7acetyl-amino-L-hydroxy-naphthalene-3, 6-disulfone acid Six tablets (0.3 grams) of sulfamilamide, were administered daily by mouth. The dosages were reduced after a tew days and discontinued on the The patient began to imeighth day prove on the third day of treatment, and within a week he appeared entirely well A similar therapeutic regime effected recovery in two cases of streptococcie meningitis recorded by M. H. Wemberg, R R Mellon and L E Shin 19 One of the patients appeared moribund prior to the institution of sulfamlamide-prontosil treatment. In both patients the prontosil was used intramuscularly, the dosage beginning at 5 cc, three times a day, and being reduced as improvement occurred Sulfanilamide was employed orally, a tablet being administered six times a day at first, and less frequently as improvement was noticed. The sulfamilamide was also used rectally in aqueous solution, the dose being equivalent to 10 or 15 grains (0.65 to 0.97 gm.) every six hours for four days One of the patients was left with a partial third nerve palsy, the other recovered completely

For meningococcic meningitis, however, the antitoxin treatment is preferred by W A Clyde and M G Neely 20 They treated ten patients with Ferry's meningococcus antitoxin, and their recovery rate was 100 per cent Each patient received an average total dosage of 50,000 units (240 cc) of this Although both the intraantitoxin spinal and intravenous routes were used. Clyde and Neely believe that the latter alone would be adequate and suggest that the spinal tap be performed only to relieve pressure, while the medication be given only intravenously While most of the patients in this series developed an urticaria, there were no instances of anaphylactic shock (See page 694 to 695 of the 1937 volume of this RE-VISION SERVICE, for a further discussion of Ferry's antitoxin)

The treatment of meningococcic meningitis by the hypodermic administration of the patient's own cerebrospinal fluid is recommended by J. S. Weiner and 5 F Bakkal 21 Of 19 patients treated with polyvalent vaccine, 15 died On the other hand, only five of the 24 patients receiving subcutaneous injections of their own spinal fluid, died

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MIGRAINE

By Eli Marcovitz, M D

No new advances have been made either in the treatment or the pathogenesis of migraine All sorts of measures are still tried in its treatment Undoubtedly the greatest advance in the past few years has been the use of ergotamine tartrate in the treatment of migraine This has now come to be the accepted treatment of this disorder, and gives good results in most cases Other methods of treatment are still widely used, especially endocrine therapy, but none of these are specific

Treatment—H S Rubinstein¹ uses trichlorethylene inhalations for patients with migraine, on the hypothesis that the headache was related to the dura, which is preponderately innervated by the trigeninal nerve. This drug has been used for some time in tic douloureux because of its anesthetizing action on the trigeninal nerve. The author reports on the use of trichlorethylene on six patients with migraine over a period of a year. At the onset of an attack the patient reclines on a bed (since in many instances inhalation of the drug produces momentary loss of consciousness) and inhales the contents of a crushed ampoule (15 minims, 09 cc) In all six cases the drug had a beneficial effect, aborting the attacks and prolonging the intervals between attacks

W M Moffat2 reports on the treatment of 17 women with menstrual migraine by the use of a gonadotropic extract of pregnancy urine. The author used the following routine ginning on the fifth to the seventh days after the onset of the menstrual flow a small dose, usually ranging from two to six rat units, was given, the dose was increased slightly daily until the tenth day, then increased rapidly, reaching a maximum of from 50 to 125 rat units on the fourteenth day. After this from 25 to 50 units was given daily until the onset of the next menstrual period These monthly courses of treatment were repeated as long as necessary

This treatment was based on the hypothesis that a leading factor in the production of menstrual migraine was either an ovarian or an anterior pituitary dysfunction, probably the former, associated with an anterior pituitary hyperfunction

With this treatment the author produced relief in all 17 cases

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MULTIPLE SCLEROSIS

By Eli Marcovitz, MD.

The past year has seen no startling advances in our knowledge of the treatment of multiple sclerosis No specific therapy is available, and of the many symptomatic methods quinine hydrochloride by mouth, and fever therapy in suitable cases offer the best possibilities Because of the relation of B avitaminosis to many sorts of nervous disorders, there has ben a tendency in the past year especially, to treat multiple sclerosis by means of diet high in vitamin B These efforts have not been successful in themselves, but it has become more or less routine to prescribe high vitamin diets for multiple sclerosis on a purely empirical basis. As for pathogenesis, recent work tends to regard multiple sclerosis as a demyelinating disease in which the patches of demyelination and sclerosis result from venous thromboses which occur from a number of causes

Symptomatology — Effect of Heat and of Cold—D J Simons¹ inquired into the effects of heat and of cold upon the muscle strength, spasticity, numbness

and bladder symptoms of 21 patients with multiple sclerosis. He presents his finding in the tables below

The author concludes that heat makes most "multiple sclerotics" weak, and that cold has no particular effect

Treatment-On the hypothesis that multiple sclerosis is a deficiency disease, A Goodall and J K Slater² have treated patients with multiple sclerosis by means of high vitamin diets. The diet recommended consists of liver (not raw) ½ pound two or three times a week, as well as eggs, milk, fresh vegetables and fruit The cereals (oatmeal, what and rice) are restricted or omitted from the diet on the basis of work by Mellanby which has shown that vitamin D (and possibly others) is antagonised by feeding animals on certain cereals No other restriction of diet is made They also recommend non-fatiguing exercises for any motor disability which may be present

The authors report on 50 consecutive cases treated in the above manner

| Symptom | Made Worse | | Unchanged | | Improved | |
|--|------------|----------------------|---------------------|----------------------|------------------|---------------------|
| | Cases | Per Cent | (ascs | Per Cent | Cases | Per Cent |
| Strength Spasticity Numbness Bladder symptoms | 13 5 2 2 | 62 24 10 10 | 5 14 18 16 | 24 66 85 76 | 3 2 1 3 | 14 10 5 14 |

| Symptom | Made Worse | | Unchanged | | Improved | |
|--|------------------|----------------------|----------------------|----------------------|------------------|---------------------|
| Symptom | Cases | Per Cent | Cases | Per Cent | Cases | Per Cent |
| Strength Spasticity Numbness Bladder symptoms | 3 5 6 6 | 14 24 29 29 | 10 10 15 12 | 48 48 71 57 | 8 6 0 3 | 38 29 0 14 |

Nine cases of less than a year's duration were reported at work, six of them had been observed from two to five years. Of nine cases with a duration of one to two years, six were working and all had improved There was only one relapse in a patient who had begun to improve and had held to the diet. One patient died, three were reported in status quo Three were reported worse, all of these were among the advanced cases of over two years' duration before treatment

Even in the group of cases with advanced symptoms of more than two years' duration, 14 of 20 patients were reported improved over a period of observation from one to four years.

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MYASTHENIA GRAVIS

By Eli Marcovitz, MD

Real progress has been made in the treatment of this disease in the past few years, and almost equal progress has been made in our understanding of its pathogenesis The symptoms of myasthenia gravis have been attributed to a disturbance in the physico-chemical mechanisms at the myoneural junction, or the motor end plate in muscles It has become increasingly apparent that the utilization of acetyl-choline at this junction is interfered with, and that the liberation of acetylcholine during muscle metabolism is an important feature of normal muscle function. The clinical and chemical studies in invasthema gravis during the past few years seem to indicate that in this disease there is a more rapid destruction of acetyl-choline than occurs in the normal person, and that the disturbance lies probably at the invoneural junction. The latter point is not yet determined definitely, but most of the evidence seems to point in this direction. It has been found that prostigmin, a derivative of physostigmine, is extremely efficacious in the relief of this tendency, and the past few years have seen a great advance in the treatment of myasthenia gravis by means of

this drug The effect is not lasting; the drug must be given indefinitely, but when given it affords great relief in most cases It may be given by injection or by mouth Injection treatment may be followed by oral administration which has been found to be just as efficacious as the injection treatment in most cases The dosage must be worked out as an individual problem. The side effects may be controlled usually by the simultaneous administration of atropine

Diagnosis-G D Gammon and H Scheie¹ studied the effects of administration of prostigmin in many types of muscular weakness such as myasthema gravis, progressive muscular dystrophy. myotonic dystrophy, family periodic paralysis and amyotonia congenita, as well as in normal adults and children

In normal persons, as well as in all cases of muscular disease except myasthenia, prostigmin in doses ordinarily employed in the treatment of myasthenia gravis sets up marked fibrillary tremors, especially in the eyelids and tongue The cases of myasthenia did not show these tremors, but showed the usual spectacular relief of weakness. The weakness present in the other conditions was

either not materially affected, or, in some cases, was slightly increased

The authors conclude, since others have shown that weakness due to lesions in the central and peripheral nervous systems is not materially improved by prostigmin, that prostigmin appears to be specific for the weakness of myasthenia gravis, since it relieves no other condition so far examined. It may be used as a means of differential diagnosis of myasthenia gravis from other conditions.

A M Harvey and M R Whitehill² also found that prostigmin seemed to be of value in the diagnosis of myasthenia gravis, since the administration of a single dose of prostigmin in 14 cases of other neurologic and muscular disorders produced no immediate improvement

Prostigmin Poisoning-L S Goodman and W | Bruckner | report a personal experience after taking orally 34 grain (45 mg) of prostigmin. The recommended oral dose of prostigmin in invasthenia gravis is 12 grain (30 mg) three times a day (10 to 30 times the subcutaneous dose) and even larger amounts have been used In the case reported all the classic signs of physostigmine intoxication occurred. The heart rate fell from 78 to 65 in 30 minutes, and reached its lowest rate (63) in one and one-half At this time salivation was hours There was a long latent first noted period of 90 minutes between salivation and sudden onset of shock, with a feeling of fluttering in the abdomen, diaphragm and thorax, difficulty in breathing, severe giddiness, faintness, fear of impending death, cold sweating of extremities, pallor, then twitchings involving the entire skeletal musculature, and violent intestinal movements. Miosis and difficulty in accommodation also oc-Intermittent exacerbation of curred

symptoms occurred, and fainting was forestalled only by the greatest efforts. The administration of atropine brought relief in about 30 to 45 minutes.

On the basis of this experience the authors warn against the oral use of prostigmin in the usual high dosage, until much more is known about its fate in the intestinal tract. They recommend that for the present it be given parenterally, so that the dosage can be controlled

Treatment-Melvin W Thorner and Joseph C Yaskın4 have treated myasthenia gravis with various forms of therapy and report as follows cases of myasthenia gravis were treated by various methods Glycine in ½ounce (15-Gm) daily doses for periods varying from two weeks to three months produced no symptomatic change Prostigmin was given orally and the dosage to each case so adjusted that each dose produced an effect lasting one to four All the cases were strikingly benefited \ll arrived finally at the same dosage, namely five to nine 1/4-grain (15-mg) tablets evenly spaced throughout the day. As function of the myoneural junction is presumed to be dependent upon acetylcholine in the structures, potassium chloride was tried and resulted in no improvement Four of the five cases showed slight but definite improvement with ephedrine capsules, 35-grain (24-mg), taken two to four Benzedrine was found times a day useful as an adjuvant to prostigmin Roentgen therapy over the thymus gland in three patients resulted in no significant change"

R S Mitchell⁵ reports on the use of **prostigmin by mouth** on nine patients with myasthenia gravis. In every case the beneficial effect was greater than with any previous medication, including ephedrin, glycin and parenteral prostig-

min All of these patients became able to get along at home without continuous medical supervision. The average daily dose was 1½ grains (90 milligrams), divided over five or six doses. The author recommends that they be timed so that meals are taken about 30 to 40 minutes after a dose. He also stresses the importance of adequate rest.

Various untoward effects of this treatment were observed, including nausea, salivation, perspiration, dizziness, loose bowel movements, occasional muscular aches and pains, and rarely, abdominal cramps, vomiting and diarrhea None of these symptoms last for more than 15 to 30 minutes. The simultaneous administration of ½000 or ½150 gr (0 32 or 0 43 mg) of atropine sulfate or 10 to 30 minims (0 6 to 2 cc) of the tincture of belladonna effectively abolishes these symptoms

Five of the nine cases seemed to be benefited by the simultaneous administration of $1\frac{1}{2}$ to 3 drains (6 to 12 Gm) of **potassium chloride** daily Two of these felt that prostigmin had little effect without it. In four cases the simultaneous use of potassium chloride made no difference

N W Winkelman and M T Moore⁶ report on the use of prostigmin in six cases of myasthenia gravis, six cases of muscular dystrophy, and one case of amyotrophic lateral sclerosis. In order to prolong the action of the drug in myasthenia over the entire day and to obviate the untoward parasympathetic effects of a single large dose, the authors recommend doses of 15 minims (1 cc) three times a day hypodermically. In the muscular dystrophies the authors report that in the early stages of this

malady the effect of the drug was to improve muscular power, but in late stages no improvement was noted. They believe that a prolonged period of study is necessary in this group before definite conclusions can be drawn. In their case of amyotrophic lateral sclerosis use of the drug was followed by marked increase of the fibrillary tremors.

J W Macfarlane⁷ reports on two cases of myasthenia gravis who were treated with injections of prostigmin and later maintained on glycine and ephedrine There was the usual dramatic response to prostigmin, with the ensuing relapse after the effects wore off After the patients were relieved by prostigmin, $\frac{1}{4}$ ounce (7.5 Gm) of glycine and ½ grain (32 mg) of ephedrine sulfate were administered once or twice daily In one of the cases the prostigmin was continued for some time and then dis-The author found that pacontinued tients were able to get along successfully on glycine and ephedrine, and that a gradual reduction in dosage was possible after the full effects were obtained He tentatively suggests that a course of prostiginin may be of advantage before commencing the glycine and ephedrine therapy

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MYOPATHIES

By Eli Marcovitz, MD

There has been little which is new in the past year to throw light on the myopathies In recent years the emphasis has been upon the role of muscle metabolism in the development of various types of myopathy In some myopathies there has been found a definite increase in creatine excretion in the urine, and a disturbance in the metabolism of creatine-phosphoric acid in muscles Thus far, no specific findings have been found to be associated with specific myopathies At present it is not possible to go further than the general assertion that there is in many myopathies a disturbance of muscle metabolism

Treatment of the myopathies still remains largely symptomatic. Because of the disturbance in protein metabolism in the muscles, the amino-acid glycine has been given in large quantities to myopathic cases. It has been of benefit in some cases, but on the whole the results with this form of therapy have been quite disappointing. It is used empirically but it is not always beneficial Benzedrine sulfate and ephedrine sulfate have also been used but with indifferent success. Much remains to be learned about this group of disorders

Treatment—Foster Kennedy and A Wolt¹ report on four additional cases of invotoma atrophica who responded to quinine hydrochloride, 5 to 10 grains (0.32 to 0.65 cm.) three times a day by mouth. The authors conducted experiments on patients with myotoma and myasthema, administering various pharmacological products, especially quinine and prostigmin. They found that these drugs appeared to be antagonistic, the prostigmin increasing the myotoma, while quinine exaggerated the myasthenic symptoms. The authors also distinct the prostigmin increasing the myotoma, while symptoms.

covered that other drugs and endocrine products, viz, ephedrine, epinephrine, atropine, glycerin, thymus, anterior pituitary, thyroid, parathyroid, viosterol, calcium and insulin produced contrasting effects on these two diseases They conclude from their work that myasthenia and myotonia are primary disorders of muscle or of the myoneural junction, that prostigmin facilitates the action of the so-called "vagus stuff" in myasthenia, and that quinine inhibits this action in myotonia, at the myoneural junction, and that little understood endocrine disorders are at work in the maladies

S Hurwitz,2 in a discussion of primary myopathies states that he treated 12 patients with from 4 to 30 Gm of aminoacetic acid daily for from 6 to 25 months Subjective improvement occurred in seven cases (583 per cent), featured by an increase in appetite, a gain in weight and a feeling of well-being Patients apparently could do more because of the decreased fatigability of the muscles involved At the time of writing, the condition seemed to be airested in two patients, in two others the course had apparently been slowed, one died while receiving treatment, and the others had received no appreciable benefit

The author concludes that the use of ammo-acetic acid causes no striking improvement in the majority of cases, particularly if the condition has begun in early life. Continuation of this therapy is warranted however, because of the subjective improvement, and the possibility that the disease may be arrested

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NEURITIS

By J C YASKIN, M D.

Vitamin Deficiency and Neuritis

Significant advances in the etiology, pathology and especially the treatment of multiple neuritis have been made in recent years through the investigations of deficiency diseases, especially avitami-F H Lewy¹ gives a general survey which is practical for clinical orientation His presentation, which is based on clinical observations and neurologic and chemical examinations, started with the observation that despite the wide clinical variety of peripheral nerve diseases, their histopathologic features are uniform Primary inflammatory processes of the peripheral nerves are unknown Therefore the term neuritis is erroneous and should be replaced by neuropathy With refined methods of examination, such as graduated hairs and thorns and chronaximetry, neuropathies can be demonstrated in many exogenous and endogenous intoxications and infectious Their appearance is accomdiseases panied by the increase of ketones and pyruvic acid in the blood and urine Both these products point to a disturbance in the intermediary carbohydrate The increased output of metabolism ketones indicates the gradual depletion of glycogen in the liver, and the increase in pyruvic acid seems to be a direct consequence of the absence of vitamin B

The pathogenic mechanism of the neuropathy seems to be as follows. First, various primary etiologic agents—infectious, toxic and metabolic—act on the liver. The liver cell becomes depleted of its glycogen and, simultaneously, of its vitamin B content. Then the stage is set for a neuropathy. Second, B avitaminosis appears as the only form of neuropathy. However, the neuropathy is not the only sign of B avitaminosis.

In addition, there are: (1) The socalled general symptoms, (2) physical signs and (3) evidence of systematic degeneration in the spinal cord and basal ganglia.

From an experimental standpoint, lessons in the nervous system have been produced by the absence of:

- 1 The fat-soluble vitamin A the lack of which produces degeneration of the medullary sheaths of the peripheral nerves and of the ascending, chiefly the spinocerebellar, tracts of the spinal cord.
- 2 The water-soluble, heat-labile antineuritic vitamin B_1 —the lack of which in animals produces the clinical and pathological changes resembling beriberi in man
- The water-soluble, heat-stable vitamin G or B2-a lack of which in animals produces clinical and pathological changes similar to those observed in human pellagra H M Zimmerman, G R Cowgill and J C Fox, Jr 2 summarize their experiments as follows The basal diet employed in this study consisted of an artificial balanced ration which was palatable to the dog and adequate in all known dietary essentials except watersoluble, heat-stable vitamin G (B2) The experiment was controlled by feeding a second group of dogs the same diet plus an adequate amount of vitamin G (01 Gm of liver extract per kilogram of body weight daily) A third group of animals served as controls for the inanition factor, each animal was fed daily only as much of the basal ration as his experimental partner had eaten on the preceding day plus an adequate amount of vitamin G

During the first stage of the experiment the animals were taught to walk on their hind legs, hurdle an obstacle

board and maintain their balance on a turntable Repeated examinations of the neurologic status were made throughout the experiment, and frequent cinematographic records were obtained of the 15 dogs maintained on the ration deficient in vitamin G a slowly progressive disease developed, characterized by loss of weight, vomiting and bloody diarrhea, flaccid muscular weakness, incoordination and decrease of the deep reflexes Death occurred in from 107 to 599 days. It was found that the acute symptoms could be modified and the life of the animals prolonged by the administration of a minimal amount of vitamin G-0.05 Gm of liver extract per kilo-This pergram of body weight daily mitted the gradual development of the neurologic signs to a more marked degree. In each of the 12 control animals which received an adequate amount of vitamin (a there failed to develop either the clinical or the pathological manifestations of the disease. The lesions consist of marked demyelmization of the peripheral nerves and degeneration of their axis-cylinders. Many medullary sheaths and axis-cylinders of the posterior colunns are also destroyed and replaced by gliosis. These degenerative changes in the nervous system are similar to those observed in cases of human pellagra

From a clinical standpoint vitamin deficiency is exhibited, in addition to pellagra and beribert, in cases of (1) alcoholic neuritis, (2) polyneuritis of pregnancy (3) "gastrogenous" neuritis and (4) diabetic neuritis

1 **Recholic Polyneuritis—N Jolliffe and S N Colbert point out that vitamin deficiency may be an etiologic factor in the development of polyneuritis in the alcohol addict. The alcohol addict selected for this study had polyneuritis. Patients having complications likely to increase the vitamin B requirement or

to prevent absorption from the gastrointestinal tract or utilization of vitamins (pneumonia, tuberculosis, hyperthyroidism, delirium, vomiting, diarrhea, pellagra, clinical icterus and ascites) were excluded from this study. Palpable liver, dependent edema, low grade fever, achlorhydria, anemia, anorexia or a psychosis not associated with delirium did The selected panot cause exclusion tients were placed in rotation into groups A, B and C until 23 subjects were studied, then five successive patients were placed in group C, making a total of 28 subjects All the subjects were given physical therapy, and symptomatic treatment was given as occasion required Group A The seven patients in this group were given a basal diet estimated to contain 2190 calories and 3680 mg equivalent (736 Sherman units) of vitamin B Group B eight patients in this group received the same basal diet as those in group A, but in addition they were given 18 Gm of unheated Vegex daily Vegex contains about 225 mg equivalent (45 Sherman units) of vitamin B per gram This added 4050 mg equivalent of vitamin B to the basal diet Group C The 13 patients in this group received a vitamin-rich diet estimated to contain 3100 calories and 17,250 mg equivalent of vitaniin B To this diet was added 18 (im of Vegex daily The authors state that patients receiving borderline amounts of vitanin B showed no improvement in the objective signs of peripheral neuritis over a period of a month Two of these subjects were then given crystalline vitamin B₁ by intravenous injection, with dramatic response in one and a good response in the other Subjects treated with a vitamin B intake approximately twice their preducted reguirement showed improvement, but not as rapidly or to the same degree as those receiving four times their vitamin B requirement. The authors conclude that (1) alcohol per se is not the cause of polyneuritis in the alcohol addict. (2) Vitamin B deficiency is a cause of polyneuritis in the alcohol addict.

2 Polyneuritis of Pregnancy-This disease usually occurs in the second month and, while usually mild at the beginning, becomes pernicious in type Dehydration and emaciation result from the vomiting The onset of paralysis is usually during the third and fourth The customary complaints are numbness, weakness and increased muscle pains, generally in the lower ex-Mental symptoms similar to tremities Korsakow s psychosis appear at about the same time as the neurologic changes The mortality of polyneuritis of pregnancy is about 25 per cent This can be reduced considerably by the early recognition of the disease and the administration of a proper diet or by the interruption of pregnancy Since the disease is due to lack of vitamin B, large amounts of this vitamin should be given as soon as the symptoms of polyneuritis are recognized. In fact, in all cases of hyperemesis gravidarum it is advisable to give vitamin B prophylactically For patients who do not respond readily to vitamin B, M B Strauss and W McDonald4 recommend liver and liver extracts both by mouth and by injection If patients fail to improve under this therapy, the pregnancy should be terminated If this is done too late, it will not prevent death

3 "Gastrogenous" Polyneuritis—A H Douthwaite' studied seven patients with polyneuritis in whom the only constant feature was disturbance of gastric function, there was either reduction or absence of free hydrochloric acid. The current conception concerning achlorhydria and achylia is that in most cases

this condition appears as the terminal result of chronic gastritis. When atrophy of the mucous membrane of the stomach and possibly of the first portion of the duodenum becomes complete, pernicious anemia and subacute combined degeneration are likely to arise, owing to absence of the as yet unidentified substance known as hemopoietin and neuropoietin. In some cases of subacute combined degeneration there is evidence of polyneuritis, and it seems reasonable to suspect that the health of the peripheral nerves is, like that of the spinal cord, dependent on an adequate supply of neuropoietin or of some allied substance secreted by the gastric and the duodenal mucosa

In view of the cases observed, Douthwaite feels justified in postulating the possibility of the existence of gastrogenous polyneuritis. Three of the patients presented a slightly modified blood picture and were given therapy for anemia with hydrochloric acid, all improved within a few months and remained well, two had definite gastrointestinal defects, correction of which resulted in cure. The other two patients had gastric carcinoma.

The most important aspect of avitaminosis in relation to nervous diseases is its value in therapy Heiman's reports 30 cases in the treatment of which he resorted to a preparation of vitamin B₁ The clinical histories of 15 of these cases are reported in detail. He thinks that the injection of the B₁ preparation is indicated in all disturbances of the peripheral nervous apparatus. On the basis of theoretical reasoning, he differentiates two groups of nervous diseases group includes those disorders in which a deficiency of vitamin B₁ is presumably The author includes in this involved group polyneuritis caused by alcohol, lead, thallium, arsenic, diabetes, beriberi, pellagra, carcinoma, pregnancy, edema due to starvation, and manition Al-

though it may not be possible to demonstrate an absolute or relative vitamin deficiency in all these conditions, there are nevertheless indications of a relationship to avitaminosis The second group of disorders includes those peripheral nervous disturbances in which pain predominates or plays a part. It has been found by experience that these disorders respond to vitamin B₁ favorably Since vitamin B₁ shows a great affinity for the centripetal than for the centrifugal nerves, its application is especially suited to disorders that involve chiefly the Central nervous dissensory nerves turbances such as myelitides, funicular myelitis, multiple sclerosis and heredodegenerative diseases, do not respond to treatment with vitamin B1, according to the author's experience He suggests that in the initial stage of multiple sclerosis, the preparation of vitamin B₁ be tried

Diabetic Neuritis

The diagnostic and therapeutic problems of diabetes are at times very difficult and a careful study of a large group of cases is important. W. R. Jordan? examined 226 patients suffering from diabetes complicated by peripheral neuritis. The forms of the disease are divisible into three groups. Hyperglycemic cm 13 per cent of the patients), pure neuritic (in 52 per cent) and degenerative (in 35 per cent). The hyperglycome group is defined as that which embraces the mild neuritides bearing some relationship to the hyperglycemia, in which symptoms tend to diminish as the diabetes is controlled. The neuritic group includes forms in which the neuritis is stubborn and extensive, while the degenerative type embraces conditions with a circulatory or an arteriosclerotic In the hyperglycemic type, the usual site of involvement is the lower extremity, and the outstanding symptoms are pain and cramps, which are worse at night. There is little arteriosclerosis and the symptoms appear when the diabetes is uncontrolled, tending to vanish as the blood sugar is restored to normal. No special treatment of the neuritis is required, as the pain and cramps are controllable by any measures which control the underlying diabetes.

In the neuritic type pain is severe, and paresthesias, changes in the reflexes, areas of muscular weakness and scattered neurologic signs usually develop Pain is worse at night and improves when the patient walks In most cases the tendon reflexes are diminished or absent Muscular weakness is found in most cases, there may be complete paralysis of a muscle group, although usually there is only paresis. Atrophy is often Tenderness, hyperesthesia and alterations in objective cutaneous sensibility are found in slightly more than half of the cases Little alteration in position sense is found, and ataxia is Patients in this group are often unstable, restless and depressed keystone of therapy is intensive treatment of the diabetes. The diet should be as rich as possible. If the neuritis develops shortly after the initiation of treatment with insulin, the brand of insulin should be changed, as in some cases sensitiveness to the insulin solvent may account for the disorder Pain is relieved best by heat, which is applied in the form of warm baths or an electric baker Massage. Buerger's exercises and a program of alternating rest and exercise should all be tried

In the degenerative type the onset is insidious. In most cases the extremities are involved, although pupillary changes are also frequent. There are paresthesias, cramps and pain—all worse at night Among the neurologic findings are

changes in reflexes, atrophies, weakness of the anal sphincter, tenderness of the muscles and areas of hyperesthesia. In every case some degree of arteriosclerosis is found. The course is prolonged, and the symptoms may persist. Heat is a

valuable anodyne but must be applied with care because of the danger of burns. The electric baker is advised. Meticulous care must be taken in trimming nails, corns and calluses. Buerger's exercises should be used in all cases.

NEUROSYPHILIS

By J C Yaskin, M D

Asymptomatic Neurosyphilis

The campaign for the prevention and treatment of all forms of syphilis, instituted by the United States Public Health Service, under the able direction of Surgeon General Thomas Parran, is reflected especially in neurosyphilis In the first of a series of reports on neurosyphilis to be published by the cooperative clinical group, P. A. O'Leary, H. N. Cole, J. E. Moore, J. H. Stokes, U. J. Wile, T. Parran, R. A. Vonderlehr and L. J. Usilton¹ asymptomatic syphilis is discussed

Asymptomatic neurosyphilis is characterized by a positive reaction of the spinal fluid in the absence of objective or subjective symptoms of involvement of the central nervous system. Its importance lies in the fact that it is the precursor of the clinical forms of neurosyphilis and that it is amenable to treatment. The records of the cooperating clinics contain 712 cases of asymptomatic syphilis, and they form the basis of this report.

The only diagnostic means for asymptomatic neurosyphilis is a complete examination of the spinal fluid, which consists of a complement fixation or flocculation test, a cell count, and a colloidal gold, benzoin or mastic test

In early syphilis the spinal fluid should be tested early in the course of treatment and certainly by the sixth month. If normal, the test should be repeated at the completion of treatment. If the first test is positive, subsequent tests should be made at intervals of three months during the course of treatment to note the trend of the fluid. A patient with early syphilis who, at the sixth month of regular and adequate treatment, has a normal spinal fluid may be reassured that the latter will not become positive as long as the blood Wassermann remains negative. However, at the completion of treatment the fluid should be re-examined.

In late syphilis, a spinal fluid test should also be made early in the course of treatment. If the spinal fluid is abnormal, re-examinations are necessary at the beginning of each arsphenamine course, in order to establish the trend of the fluid as a guide to treatment.

If the blood and spinal fluid become normal, the fluid should be re-examined the first and the third year after the completion of treatment

The character of the spinal fluid is a clue to the prognosis and a valuable guide in the program of treatment. Patients with less severe types of spinal fluid involvement respond more readily and require less treatment than those whose fluid indicates general paresis.

Asymptomatic neurosyphilis was demonstrated in 13 5 per cent of 5293 syphilities whose spinal fluid was examined

White adults are more prone to develop asymptomatic neurosyphilis than negroes. The incidence of asymptomatic neurosyphilis decreases and that of clinical neurosyphilis increases with the duration of the infection. Extragenital chancre, even if located above the neck, does not predispose to neurosyphilis.

The scheme and amount of treatment given during the early phase of the infection are potent factors in the development of asymptomatic neurosyphilis. Patients who received an adequate amount of treatment (20 or more injections of arsphenamine plus 20 injections or the equivalent of a heavy metal) administered by the continuous system at the early stage, showed the lowest incidence of asymptomatic neurosyphilis. Of patients treated adequately but irregularly, 22.6 per cent had asymptomatic neurosyphilis

A negative blood Wassermann reaction does not obviate the need for a test of the spinal fluid in 14 per cent of the blood-negative cases the spinal fluid was positive. Of the patients who had been adequately treated for early syphilis and who had a negative Wassermann reaction of the blood, 17.1 per cent had asymptomatic neurosyphilis A persistently positive Wassermann reaction in the blood was associated with abnormal spinal fluid in 75 per cent of cases. In latent syphilis of four or more years' duration a normal fluid remained normal in 99 per cent of the cases, irrespective of the Wassermann reaction of the blood

Of the 712 patients, 565 were treated and observed for two years or more and had two or more spinal fluid tests. By the end of the fifth year of treatment, routine therapy had reversed to normal 246 per cent of the spinal fluids, intraspinal therapy had added 241 per cent, tryparsamide five per cent, malaria therapy 28 per cent, and a combination of

all methods 07 per cent Another computation shows that normal spinal fluids were obtained by the end of the fifth year in 685 per cent of patients treated by the routine method, 683 of those treated by the routine and intraspinal methods, 593 of those treated by the routine method and tryparsamide, and 195 of those treated by the routine method and malaria therapy These figures do not give a numerical estimate of the value of the various therapeutic agents, since routine treatment was tried first, intraspinal or tryparsamide therapy was added only in resistant cases, and malaria was employed only where other methods failed

Frequency, Prognosis and Treatment of Positive Spinal Fluid in the First Year of Syphilis

Closely related to the subject of asymptomatic neurosyphilis is the long recognized fact that the nervous system may be invaded carly in the course of syphilis August Matras² reports that among 721 patients who had not been treated and in whom lumbar puncture was performed during the first year of the infection when they were in the primary or early secondary stage 95, or 13 per cent, showed positive spinal fluids Of these 64 were men and 31 women Of the 64 men three were in the seronegative primary, ten in the seropositive primary and 51 in the early secondary stage One man out of four in the early secondary stage had a positive spinal fluid Among the women one was in the seropositive primary stage and 30 in the early secondary stage

The degree of the changes was generally mild but in some of the early secondary cases they were moderately or strongly positive. In some of the early secondary cases there were neurologic

changes, chiefly in the form of signs of meningeal irritation

The milder cases are generally transitory but it is always impossible in any given case to say whether it will become permanent or not

Two systems of treatment were used in these cases—in one group a comhined arsenic-bismuth treatment and in the other malaria treatment cases treated with arsenic and bismuth 50 per cent were restored to normal while in those treated with malaria the spinal fluid was rendered normal in 80 per cent Some of the cases treated with arsenic and bismuth were mild and one of the patients treated with malaria proved to have multiple sclerosis, showing that positive spinal fluid findings are occasionally not caused by syphilis The re-examinations were made from one to five years after the changes were first demonstrated

The author concludes that cases of syphilis with positive spinal fluid changes in the first year should be treated with malaria. Chemotherapy alone is not sufficient to guarantee these patients against the late results of syphilis.

The Incidence of the Clinical Types of Neurosyphilis in Males, in Pregnant and in Non-Pregnant Females

W C Menninger and J E Kemp's examined four hundred cases of neuro-syphilis, 100 nullipara, 100 multipara, and 200 males Thirty-eight per cent of the males had asymptomatic neuro-syphilis. 56 per cent parenchymatous, and six per cent meningovascular neuro-syphilis. Among the nullipara, 63 per cent had asymptomatic neurosyphilis, 29 per cent parenchymatous, eight per cent meningovascular, 54 per cent of the multipara had asymptomatic neurosyphilis.

ilis; 38 per cent parenchymatous, eight per cent meningovascular neurosyphilis.

Acute Syphilitic Meningitis

Inflammation of the meninges to some extent is found in *all* forms of neuro-syphilis. The clinician usually regards syphilitic meningitis as a chronic or at most as a subacute process. The existence of *acute* forms is not often thought of and is probably frequently overlooked. Three contributions to this subject deserve consideration.

H H. Merrit and M Moore⁴ summarize an extensive study as follows

1 Acute syphilitic meningitis is a relatively rare complication of syphilis as it occurs in less than five per cent of the cases It usually occurs in young adults but it may be a complication of congenital syphilis The meningeal symptoms usually develop within one year of the primary infection, but may develop at any time after the initial lesion and may be a complication of parenchymatous neurosyphilis. The symptoms have an acute or subacute development In most instances they are present two to four weeks before the patients seek admission to the hospital. The meningitis is not caused or precipitated by arsenical therapy Thirty-six per cent of our cases had no anti-luetic therapy prior to the onset of the meningitis, and the onset of meningeal symptoms did not occur in any of our patients while they were receiving arsenical therapy, nor have we found any case recorded in the literature in which the symptoms developed during arsenical therapy. They may develop, however, while the patient is receiving mercury by munction or intramuscular mjection

2 Clinically the cases divide themselves into three groups according to the presence of symptoms indicating involvement of the meninges in various

regions of the brain as follows acute syphilitic hydrocephalus; cases with headache, nausea and vomiting, choked discs and meningeal signs (stiffness of the neck and Kernig's sign) indicating involvement of the meninges in the posterior fossa interfering with the circulation of the cerebrospinal fluid and causing the development of an acute hydrocephalus, (2) acute vertical meninuntis, cases with headache, nausea and vomiting, convulsions or mental symptoms indicating involvement of the meninges over the vertex of the brain, (3) acute basilar meningitis, cases with cramal nerve palsies indicating involvement of the meninges at the base of the brain

3 The blood Wassermann test is positive in only 60 per cent of the cases and is an unreliable test in excluding the diagnosis of acute syphilitic meningitis. The cerebrospinal fluid findings are characteristic, and the diagnosis can be immediately established only by lumbar puncture. The cerebrospinal fluid is usually under increased pressure, which nay be as high as 600 to 700 mm There is moderate or marked pleocytosis (25 to 2000 cells per cubic millimeter) Lymphocytes are the predominating cell type but 5 to 15 per cent polymorphopuclear leukocytes are usually present and rarely they may predominate. The protein content of the fluid is increased The glucose content may be normal or decreased (18 to 84 mg per 100 cc) The chloride content is usually normal or only slightly decreased (636 to 742 mgm per 100 cc) The colloidal gold reaction is practically always abnormal and may be of any type. A mid zone curve is found in 50 per cent and a first zone in 40 per cent. The cerebrospinal fluid Wassermann is positive in approximately 90 per cent Spirochetes have been found in the fluid

4 The pathological findings are a nonspecific reaction to the treponema pallidum The meninges are infiltrated with lymphocytes, plasma cells and occasionally polymorphonuclear leukocytes There is a slight degree of perivascular infiltration of the meningeal and superficial cortical vessels Occasional small areas of cortical softening are found as a result of thrombosis of vessels showing peri- or endarteritis

5 The treatment of acute syphilitic meningitis consists in the *intravenous injection of arsphenamine* (or its derivatives) and *frequent lumbar punctures* Under this treatment the acute symptoms rapidly subside. The ultimate prognosis is good (87 per cent) when the proper follow-up treatment is given. The prognosis is poor (34 per cent) when no treatment or inadequate treatment is given. Parenchymatous neurosyphilis (tabes dorsalis and dementia paralytica) may develop as a sequel to acute syphilitic meningitis.

Acute syphilitic meningitis is especially apt to be overlooked in the presence of fever when bacterial meningitis is usually suspected, or when occurring in association with suppurative otitis when the absence of organisms suggests the existence of a brain abscess. Two such cases are reported by Roma Amyot 5. The author describes such a case in a young man 23 years of age who came to the hospital with such intense headache that rest and sleep were impossible. He had a history of chronic suppurative otitis on both sides for two years and hearing was impaired on the left side There was considerable meningeal reaction of the lymphocytic type without the typical clinical signs of meningitis but with marked signs of intracranial hypertension, the patient was in very poor general condition and had a partial left hemiplegia A cerebral abscess of the right temporal region originating from the otitis was suspected. Ventriculography, however, showed the absence of abscess. In the meantime the report of the lumbar puncture showed positive Wassermann, benzoin, and colloidal gold reactions. The patient had become able to give a history and said that about nine months before he had had a small swelling on the glans and enlargement of the inguinal glands. He had been given three series of intravenous injections probably of novarseno-benzol, it was three weeks after the last of these that the meningitis began

Another patient, a woman of 47, was admitted to hospital with violent headache The previous month she had had three attacks with loss of consciousness. tonic convulsions, and blueness of the There was no history of sinusitis, otitis, coryza, or tonsillitis She too had signs of intracranial hypertension with bilateral choked discs, the spinal fluid showed a lymphocytic type of inflammation without bacteria, and a slight paresis of the left limbs as a sign of localization on the right side. These signs too suggested cerebral abscess but remembering the previous case the blood and spinal fluid tests were made at once and both were strongly positive. It was evidently a case of syphilitic meningitis. The patient did not remember having had any skin eruption and she had never had any treatment

In these cases of syphilitic meningitis the meningeal infiltration interferes with the flow of spinal fluid and so brings about the signs of intracranial hypertension. The typical signs of acute meningitis such as are seen in tuberculous meningitis—Kermg's sign, rigidity of the neck, photophobia, hyperesthesia of the skin, and retraction of the abdomen—are absent or slight. There may be considerable rise of temperature.

The clinical signs of syphilitic meningitis recede quite rapidly under specific treatment. Unfortunately the spinal fluid reaction may persist and tertiary syphilis or even general paresis may develop. Patients with resistant spinal fluid should be given malaria treatment to prevent development of general paralysis.

The difficulties in the diagnosis may even be greater in congenital syphilitic meningitis in children where the acute form may closely simulate tuberculous meningitis R Debre, J Marie and A Bernard-Pichon⁶ describe a case in a child six months of age who entered the hospital for slight digestive disturbances Two days later the clinical symptoms became those of tuberculous meningitis, so much so that this diagnosis was made in spite of the fact that the skin reactions to tuberculin remained negative and roentgenograms of the lungs were nega-The mother was then questioned and admitted that her Wassermann reaction had been strongly positive during pregnancy The Wassermann and Kahn reactions were positive in the blood of the mother and in the spinal fluid of the child, finally the diagnosis of subacute congenital syphilitic meningitis was accepted and the child treated with biniodide of mercury and bismuth. After three months and a half the lymphocytosis of the spinal cord became normal and the Wassermann and Kahn reactions negative At the end of five months the child was discharged with the meningitis cured but with psychomotor retardation

This case shows that subacute congenital syphilitic meningitis may simulate tuberculous meningitis so closely as to deceive even the most skilled clinician. There may even be fever as in this case. This form of meningitis may attack the nursing infant or the older child and may end in death, complete recovery, or recovery with sequels (psychomotor re-

tardation). It is decidedly affected by antisyphilitic treatment which should be given carefully but nevertheless energetic and prolonged. A congenital syphilis with positive biologic reactions may be associated with a meningitis of tuberculous or other origin, so that a positive Wassermann reaction does not necessarily mean that the meningitis is syphilitic

Treatment of Neurosyphilis-The treatment of neurosyphilis is often difficult and complicated and a review by a keen clinician of wide experience is always valuable P A O'Leary7 states that the development of knowledge of neurosyphilis and its treatment dates back a quarter of a century this time it has been shown that one of the outstanding values of chemotherapy, with arsphenamine and compounds of bismuth of mercury, is its ability to prevent the development of neurosyphilis Of a large group of cases of early syphilis, adequate administration of these remedies prevented the appearance of neurosyphilis in 84 per cent. When the neurosyphilis was manifested, the value of chemotherapy was greatest in the asympatomatic type in which it produced excellent results in 75 per cent of the early cases, while it was practically valueless in the treatment of patients who gave evidence of well established dementia paralytica. Between these two extremes are a great number of patients with various types of neurosyphilis, in which the results of chemotherapy differ according to the duration of the syphilis and the degree and extent of involvement of the central nervous system. In those cases in which only invasion of the nervous system has occurred the results of treatment are usually satisfactory, while in those in which extensive parenchymatous and vascular involvement has occurred the results are proportionately unfavorable Accordingly, the de-

mand for a method to control the disease in the later types was met when Wagner von Jauregg recommended malarial therapy, which also has weathered the trial of time and experience in thousands of cases The effort to simplify malarial therapy resulted in the development of artificial fever therapy, first by the radiotherm, then by the hypertherm, and subsequently by a variety of means of raising the patient's temperature was at first hoped that the production of fever by mechanical methods would result in a new method of therapy, namely, the killing of bacteria within the patient Experience to date has shown, however, that this concept is applicable only in those diseases in which the thermal death point of the bacteria is low. The spirochaeta pallida has a high thermal death point, 114° F (455° C), so it would appear that the favorable results obtained in neurosyphilis by fever therapy, whatever the type may be, are the result of some biologic phenomenon the nature of which at present is not known Fever therapy in the treatment of neurosyphilis, although used empirically, should be administered in conjunction with, or immediately followed by, chemotherapy

In addition to arsphenamine, bismuth or mercury, and fever therapy, there are several other therapeutic agents which have been shown by years of experience to be of value in the treatment of neuro-Outstanding among these is tryparsamide, which, when used in conjunction with fever therapy, offers the highest incidence of clinical and serological remissions in dementia paralytica The combination of tryparsamide and a compound of bismuth is recommended in the treatment of patients with neurosyphilis who are too debilitated to undergo fever therapy, as well as in the types of neurosyphilis in which no benefit is derived from fever therapy

The value of *intraspinal therapy* is well demonstrated in cases in which there are early clinical signs of tabes or optic atrophy, and in cases of asymptomatic neurosyphilis. Intraspinal therapy should not be given when evidence indicates extensive involvement of the lower part of the spinal cord.

The less intensive types of nonspecific therapy, such as those in which are employed typhoid vaccine, hot baths, sulfur in oil, and bacterins, are applicable in those cases in which a mild nonspecific effect is desired, because in the inalignant types of neurosyphilis these remedies are less efficient than the more strenuous types of fever therapy

In addition to the use of the specific and nonspecific agents in cases of neurosyphilis, attention also must be directed toward the care of the complications of neurosyphilis, such as infected cord bladder, moreover, the development of drug addition should be avoided

As the treatment of neurosyphilis cannot be standardized, the treatment of the patient who has syphilis of the nervous system must be individualized of these patients, especially those with the early manifestations of neurosyphilis, are strikingly improved by routine therapy, and it is advisable to give them, first, the benefit of a trial with arsphenamine and a bismuth or mercury com-If there is not a favorable pound response after two such courses of treatment, the need for nonspecific therapy then should be considered However, if the patient displays early manifestations of dementia paralytica, fever therapy should be employed immediately factors that influence the decision as to the type of nonspecific treatment to adopt are the type and degree of neurologic involvement, the age of the patient, the duration of the syphilis, and the

status of the patient's general condition Fever therapy, irrespective of the type used, must be given in conjunction with, or must be followed by chemotherapy The earlier the neurosyphilis is recognized and the earlier treatment is started, the more favorable will be the effects of any type of therapy

Fever Therapy - Malaria - Fever therapy and especially malarial inoculation remain the principal agents in combating dementia paralytica In this connection a critical appraisal of ten years experience with malaria in neurosyphilis by U J Wile and E A Hand8 is of definite interest The authors report that during the period 1925 to 1935, about 474 cases of neurosyphilis were treated by induced malaria at the University of Michigan Hospital Clinic The group included 182 cases of general paralysis, 87 cases of tabes dorsalis, 54 cases of taboparesis, 80 cases of diffuse cerebrospinal syphilis, 10 cases of acute basilar meningitis, 22 cases of juvenile paralysis, 4 cases of juvenile tabes, 4 cases of combined tabes and paralysis (juvenile), and 31 cases of asymptomatic cerebrospinal syphilis The group of diffuse cerebrospinal syphilis included 14 cases in which this condition occurred in conjunction with a congenital syphilitic infection

Follow-up records were made in 354 cases. The results were evaluated with reference to blood and spinal fluid reactions, previous treatment of the patient, duration of the infection, age, sex, degree of deterioration present, height of temperature incurred, the association of herpetiform lesions, and finally the amount of antisyphilitic treatment subsequent to the malarial procedure.

The physical age of the patient seemed a more important factor than the actual age. The mortality risk reported was about three per cent. While certain contraindications to treatment were ob-

served such as obesity, cirrhosis of the liver, nephritis, cardiac disease in general, a previous history of heart failure, aneurysm, and definite aortitis and aortic regurgitation, the authors consider that the necessity frequently overrides the risk

Encouraging results were noted in selected cases of general paralysis, in the control of certain symptoms of tabes dorsalis, in diffuse cerebrospinal syphilis, in asymptomatic cerebrospinal syphilis, and in acute syphilitic meningitis. Cases of paralysis associated with congenital syphilis were not benefited by malaria treatment

The types of cases in which apparently the prognosis was best were those with acute onset and those with some treatment previous to the onset of cerebrospinal symptoms

Cases of general paralysis and tabes in which there were marked deterioration changes based upon the destructive brain and cord processes were not benefited and the symptoms of degeneration were not retarded by treatment

Encouraging results were recorded in cases of optic atrophy. Occasional slowing up or arrest of the process was noted

No striking parallelism was found between the clinical improvement and spinal fluid and blood serologic reactions. Improvement was noted coincident with fixed spinal fluid changes, and progression of the disease in occasional cases in which the spinal fluid findings had cleared up or approached the normal. The blood scrologic reactions were influenced less than the pathologic findings in the spinal fluid.

Typhoid H Antigen Vaccine—G V Kulchar and L E Anderson⁹ used typhoid H antigen in the treatment of 38 unselected patients (9 women and 29 men) with various forms of neurosyphilis. All except two pa-

tients had previously received considerable amounts of antisyphilitic treatment, and fever therapy seemed indicated because of the unsatisfactory clinical or The H antigen serologic response suspension was prepared by adding 05 per cent phenol in physiologic solution of sodium chloride to a 24-hour broth culture of motile typhoid bacilli infiltration the somatic (O) antigen was blocked off, resulting in a water-clear saline filtrate containing the flagellar (H) antigen The filtrate was standardized so that each cubic centimeter contained the flagellar antigen obtained from two billion typhoid bacilli A preliminary dose of from 40 to 50 million organisms (killed bacilli equivalent) was given intravenously by means of a 26gauge hypodermic needle Usually, but not always, a moderate chill lasting from 10 to 30 minutes occurred from 1 to 21/4 hours after the injection, at which time the patient was closely wrapped in woolen blankets and the temperature taken every half hour until it returned Increase in temperature to normal usually began at the time of the chill and required from two to three hours to reach its peak, which varied between 103° and 1056° F (394° and 409° C) The temperature remained at the maximal level from one-half to one hour, following which it gradually declined, returning to normal in from 6 to 12 hours. The rise in temperature was accompanied by an increase in pulse rate, never above 120 per minute Except for the feeling of warmth, the patients were fairly comfortable for the most part Sedatives of the barbiturate series were used to control any unusual restlessness during the period of fever The doses for subsequent injections were determined by the febrile response to the preceding dose The increases varied from 25 to 600 million per injection

After the first day, doses were divided into two portions, the second injection of the slightly lower dosage being given as soon as the temperature started to Fever was induced daily by this method until the patient had received a total of from 10 to 18 days of treatment. a day of rest usually being given after each six days of fever Each day as the temperature returned to normal the patients were allowed up about the ward. Aside from the slight loss of weight and the frequent occurrence of herpes labialis, no ill effects were observed and the patients were able to leave the hospital two or three days after completing Patients were observed for treatment periods varying from 5 to 26 months after receiving fever therapy were 285 per cent of reversals and 571 per cent of instances of marked improvement in the spinal fluid formula This compares favorably with the 367 per cent reversals and the 207 per cent instances of improvement in the spinal fluids reported by Solomon and Epstein following malarial therapy Fever therapy with typhoid H antigen provides a method that may be carried out in the home by a nurse under the supervision of a physician

Tryparsamide—Ocular Complications—Next to fever therapy, tryparsamide is at present the most potent agent in combating parenchymatous neurosyphilis, especially dementia paralytica. Since the introduction of this agent in the therapy of trypanosomiasis and of neurosyphilis attention has been called to the possibility of optic atrophy from its use. There is still no general agreement as the following contributions indicate

L L Sloan and A C Woods¹⁰ give an extensive review of studies since 1923 showing eye complications, following treatment of neurosyphilis with tryparsamide Among a total of 2087 cases treated with tryparsamide, 107 subjective reactions and 71 objective reactions were reported.

This article is based on a study of 16 patients in whom objective ocular reaction occurred after tryparsamide therapy. All of the patients had normal optic nerves, normal vision, and normal visual fields before tryparsamide treatment was begun

Only one patient showed an acute reaction to tryparsamide treatment. He became almost blind after the first injection. After forced drainage of cerebrospinal fluid the visual fields and the vision showed gradual improvement and were almost normal eight months after the reaction.

The more frequently observed chronic reactions were characterized by contraction of the visual fields with retention of normal central vision and absence of objective signs of optic atrophy There is marked tendency toward a gradual recovery from the field defect if tryparsamide therapy is discontinued Two patients were given additional tryparsamide for some time after subjective symptoms were noticed, without re-examination to determine whether objective ocular changes had also occurred Atrophy of the optic nerves developed. One patient showed reduction in vision and marked contraction of the fields which increased in severity and resulted in complete blindness at the end of seven weeks The other patient had normal central vision and moderate contraction of the fields which remained unchanged during the two-year period of observation after cessation of tryparsamide therapy

The authors concluded from their investigations that in patients with normal optic nerves, fields, and vision prior to tryparsamide therapy, there is little danger of any serious ocular damage

provided that the drug is permanently discontinued at the first appearance of the visual field defects. Continuation of the drug after changes in the fields have occurred may, however, result in serious visual damage and in complete blindness.

R S Bookhammer¹¹ reports the experiences in the men's department of the Philadelphia Hospital for Mental Diseases during 1932 and 1933 with tryparsamide and its relation to atrophy of the optic nerve The group include 262 patients Normal eyegrounds were observed in 183, 53 had atrophy of the optic nerve prior to treatment, 26 had evegrounds which made the use of tryparsamide questionable although there was no evidence of atrophy of the optic nerve. It was decided to use tryparsamide with caution in these cases. Nine of these developed atrophy of the optic Following treatment, ten of the 183 with normal evegrounds acquired atrophy of the optic nerve

M. Fine and H. Barkan¹² in treating their cases with tryparsamide decided. arbitrarily, to make a careful examination of fields, fundus and vision before the first third, fifth and tenth treatments, and before every tenth treatment thereafter Patients received weekly injections of tryparsamide. Beginning with an initial dose of 1 Gm, 2 Gm were given the second week and 3 (m) each subsequent week it no untoward symptoms appeared. The patient was questioned concerning subjective phenomena before each injection. It subjective symptoms occurred, the fields and vision were If the latter remained unchecked changed, treatment was discontinued for three weeks. The finding of any objective disturbance was considered an indication for the immediate and permanent discontinuance of tryparsamide

Under this routine, 1800 injections were given to 132 patients in a period

of about 18 months Permanent impairment of the field of vision occurred in only three patients and this was not disabling. In these three cases the follow-up was not enforced as outlined and in two instances the patient received nine treatments before the fields were checked

H P Wagener¹³ reviews the literature and concludes that the incautious use of tryparsamide in the treatment of neurosyphilis may result in a certain percentage of cases, in serious damage to the optic nerves Whether the optic nerve injury is due to a direct toxic action of the drug or to an excitation or exacerbation of a syphilitic lesion of the nerve seems relatively unimportant from a practical standpoint. The manufacturers of tryparsamide state that its use is contraindicated in cases which show opthalmoscopic or visual field evidence of optic nerve disease Apparently this dictum is not universally accepted In experienced hands it may be used safely even in certain cases of optic atrophy It should not be forgotten that visual disturbances may develop in cases with previously normal eyes Careful ophthalmoscopic and perimetric field examinations should be made in all patients who complain of disturbances of vision during the course of treatment with tryparsamide Prompt discontinuance of the drug on the appearance of the first signs of organic involvement of the optic nerve will, in most cases, prevent the development of progressive and permanent loss of vision

TABES DORSALIS

Treatment—Tabetic pains constitute a major therapeutic problem in neurology While the majority of cases yield to the various forms of intensive and prolonged treatment there are some who continued having excruciating pains

despite all forms of treatment, including the various forms of fever therapy. For these patients and in those in whom fever therapy is contraindicated, E A. Kahn and B. F Barney¹⁴ advocate anterolateral chordotomy. They report on 12 operative cases with relief of tabetic pains in eight

CHARCOT JOINTS

Medical and Surgical Aspects-While the incidence of Charcot joints has decreased markedly in the last two decades, the management of this condition, when it does occur, is always difficult S Epstein¹⁵ believes that antisyphilitic treatment alone is not sufficient to check the progress of Charcot joint disease He believes there may be some factor other than syphilis which is responsible for the joint condition occurring in apparently arrested tabetic cases He suggests that orthopedic management of a Charcot joint is more important than antisyphilitic therapy The orthopedic approach may follow radical (operative) or conservative (mechanical) lines The types of operation vary with the site and extent of damage to the joint, thus, in an ankle with marked deformity, osteotomy of the leg may correct the varus or valgus sufficiently to give considerable clinical relief A Charcot spine may be stabilized with a massive tibial graft, or the spine may be fused. In Charcot toes, the involved joints may be resected, the sinus tracts removed and the diseased bone amputated In arthropathy at the knee, arthrodesis is the operation of choice.

The conservative measures are designed to reduce pain and swelling and protect the joint from further damage. Such a regimen requires rest, immobilization (with splints, casts or braces), banning of weight-bearing movements, aspiration of fluid which may be distending the joint and use of local heat, preferably in the form of diathermy.

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PARALYSIS AGITANS

By Manuel Sall, MD

During the past year two forms of treatment have been in favor in the treatment of paralysis agitans and postencephalitic Parkinsonism Atropine sulphate and benzedrine sulphate atropine treatment of paralysis agitans has been found effective in many cases and is considered by many clinicians the

treatment of choice. Benzedrine sulphate is said by some to be effective in the treatment of Parkinsonism, especially for the symptoms of somnolence and fatigue. It is not effective alone in the treatment of Parkinsonism but should be used in connection with other drugs.

Treatment of Parkinsonism-Hyoscine and stramonium have long been the keystones of therapy in paralysis agitans In 1935 and 1936 an increasing series of reports stressed the favorable effect of atropine sulfate The chief contribution of solution. 1937 has been the recognition of the therapeutic effectiveness of benzedrine sulfate (beta-phenyliso-propyl-amine) I Finkelman and L B Shapiro¹ ascribe this response to the fact that benzedrine is a sympathomimetic drug while Parkinsonism is associated with parasympathetic stimulation. They treated 12 patients with benzedrine and atropine The dosage of the latter was 10 to 15 drops a day of 0.5 per cent (1.200) solution of atropine sulfate. The dosage of benzedrine was 13 to 12 grain (20 to 30 milligrams) a day, half the dose being given at breakfast, and half at noon They found the benzedrine very effective in reducing the frequency of the oculogyric crises, and combined with the atropine, highly successful in diminishing the tremor and rigidity Equally good results with benzedrine were secured by P. Solomon, R S Mitchell and M Prinzmetal² in cases of postencephalitic paralysis agitans On the other hand, they found the preparation ineffective in the arteriosclerotic forms of Parkinsonism eight postencephalitics with oculogyric crises, six were completely relieved of this symptom. Among 28 post-encephalitics, 26 were greatly benefited by combined stramonium-benzedrine or scopolamine-benzedrine therapy They suggest a maintenance dose of from 10 to 20 milligrams daily of benzedrine sulfate The starting dose (taken by mouth) should be five milligrams before breakfast and luncheon, this should be increased daily by five milligram increments until the maximum therapeutic effect is achieved. One of their patients was taking 160 milligrams a day for almost a month without ill effects The scopolamine hydrobromide is given in a total daily dose of 1/50 to 1/100 grain (13 to 065 mg) Instead of this alkaloid, stramonium leaves may be used, the daily dosage being 5 to 15 grains (032 to 097 Gm)

Treatment of Post Encephalitic Parkinsonism—A J Hall³ employed large doses of atropine in the treatment of chronic epidemic encephalitis. Treatment begins with $\frac{1}{12}$ grain (0.50) mg) atropine daily, given in the form of 05 per cent solution atropine sulfate administered in two doses One drop of the 05 per cent solution contains ½56 grain (0.25 mg) atropine This is increased 0.50 mg daily divided into three doses, and is continued as long as the patient presents any objective or subjective improvement When there is no further improvement, the dosage is gradually reduced until the lowest dose is obtained upon which the improvement of the patient can be main-This is the optimal dose some cases after an initial small dose has been tolerated, a greater daily increase has been made without ill effects In the authors' series, the average optimal dose was about $\frac{1}{32}$ grain (185 mg) daily The highest was $\frac{1}{10}$ grain (54 mg) daily with improvement Maximal and optimal doses, however, are not fixed points on a measurable standard, but are largely dependent upon two variables, the patient and the physician After the optimal dose has been obtained, it is convenient to prescribe the atropine in colored tablets, pink tablets contain 4 mg of atropine, yellow tablets contain 1 mg atropine. By this combination of strengths it is easy to obtain any required dose of 1 mg or upwards The patient need not be confined to bed during the treatment if he is able to be up and about When and where possible, hydrotherapy, massage and occupational therapy are invaluable adjuncts to therapy During the early part of the administration of the atropine, the patients may exhibit various discomforts Occasionally, mental confusion and slight delirium may appear shortly after taking the drug and sometimes last for one to two hours In some cases, temporary loss of memory and vertigo occur Visual disturbances due to paralysis of accommodation can be relieved temporarily by the installation of a few drops of 05 per cent eserine solution in the eves Later, more lasting relief may be obtained by the use of glasses that are adapted for the complete loss of accommodation Dryness of the mucous membranes give rise in a few cases to difficulty in swallowing Gastrointestinal upsets in the form of vomiting and acute diarrhea occur in a few cases and may be relieved by simple measures without stopping the atropine In a few cases, difficulty in starting micturition may be present

Analysis of the 58 cases treated revealed that where physical disability is maximal and psychotic disability minimal, the treatment is capable of produc-This is true ing remarkable results where the long standing Parkinsonism has not produced serious deformities of the arms, legs or trunk of an advanced nature Conversely, where psychotic disability is maximal and physical disability is minimal, the treatment is not likely to be of much benefit

Physicians are warned not to use phenobarbital (luminal) in paralysis agitans by E Ziskind and E S Ziskind,4 who find that it aggravates the rigidity Since these patients are often sleepless and nervous, the doctor may be tempted to prescribe hypnotics of the barbituric acid group But barbiturates act adversely on the basal ganglia, and the administration of phenobarbital is definitely contraindicated in paralysis agitans

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GENERAL PARESIS

By Joseph Hughes, MD

Treatment by Mosquito Inoculated Malaria-E Kusch, D F Milam and W K Stratman-Thomas1 report that patients inoculated with malaria by mosquito bite have a less severe malaria than those inoculated with blood cause of this, these patients may be subjected to a longer course of treatment and as a result gain a greater chance of a remission than those inoculated with The incubation period following mosquito inoculation is from 8 to 18 days The mosquitoes were infected with the McCoy strain of Plasmodium vivax With this strain there was usually a quotidian type of fever which ran at a peak of 104° to 106° F (40° to 411°C) The malaria attack averaged

22 paroxysms, after which the temperature returned to normal and remained there In uncomplicated cases no quinine was given until the symptoms of the malaria infection in the patient had subsided spontaneously, then 30 grains of quinine was administered daily for seven Quinine was given during the course of the fever only if symptoms of an alarming nature developed mosquito moculated malaria there was a remission rate of 264 per cent and an improved rate of 486 per cent as compared to a remission rate of 193 per cent and an improved rate of 358 per cent as seen in a comparable group of blood moculated patients

Sedimentation Rate in Cerebrospinal Syphilis

In a study of 53 cases of cerebrospinal syphilis, Fremning and Madsen2 report that an increased sedimentation rate was observed in about 50 per cent of these patients. It is contended by these authors that a low sedimentation rate and marked spinal fluid changes indicate a superficial form of cerebral syphilis which will respond favorably to treatment, while a low sedimentation rate coupled with slight spinal fluid changes indicates an older intection with a poor prognosis for remission even after fever therapy high sedimentation rate with weak spinal fluid changes usually pointed to some complicating medical problem

Lesions of the Brain Following Fever Therapy

F W Hartman' reports pathological changes observed in human beings and experimental animals incident to artificially induced fever. These consisted chiefly of acute, passive congestion of all organs and tissues and cellular degeneration and hemorrhages of the brain, adrenals, liver, lungs, and kidneys. The

author ascribes these changes as resulting from anoxia. To prevent such pathological changes from occurring, it is suggested that *oxygen* be administered to patients by means of a nasal catheter during the course of artificial fever therapy. In patients who develop an alkalosis and apnea, *combinations of oxygen* and carbon dioxide are recommended as a means of preventing the development of untoward symptoms.

Psychosis Associated with Pernicious Anemia

In a study of 255 patients with pernicous anemia, M. Herman, H. Most and N Jelliffe⁴ found 40 who presented psychotic symptoms The mental picture was not characteristic but varied in order of frequency from acute confusional states, to paranoid conditions, to affective reactions, to organic deterioration types These observers noted that an acute confusional state, occurring during a relapse of an anemia, is a sign of a critical clinical condition and should be treated by means of repeated blood transfusions until sufficient time has elapsed for specific therapy to be effective in establishing a normal blood picture

Management of Mental Reactions in Heart Disease

About ten per cent of all patients with heart disease who are sufficiently ill to require hospital care develop symptoms of a delirious nature ⁵. It is pointed out by Drewry and Wall that the occurrence of delirium is apparently conditioned by the psychological personality of the patient and precipitated usually by some severe emotional situation during the course of the illness

The first symptoms pointing to the development of mental symptoms in heart patients are restlessness at night and

irritability during the day, followed by transient periods of confusion, unsystematized paranoid ideas, fears of bodily injury and hallucinations.

Drewry and Wall feel that the excessive use of sedative and narcotic drugs contributes to the delirium and are not helpful in the management of heart patients with mental symptoms. They recommend that the treatment of these patients be directed toward the establishment of an efficient circulation by the proper dosage of *digitalis* and to the treatment of their restlessness by means of expert nursing care, in this regard prolonged baths, judiciously employed, are a helpful adjunct. If a patient is

dehydrated, sufficient fluid must be given The diet should be easily assimilated. Emphasis should be placed upon gaining the proper rest for the patient without using hypnotic drugs. *Psychotherapy* should be an integral part of any plan of therapy particularly as the patient's physical condition improves.

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PNEUMENCEPHALOGRAPHY

By Leo M Davidoff, M D

Technic-While it is generally accepted that much variation in the technical side of encephalography is possible without increasing the discomfort or danger of the procedure, work is still going forward to diminish both these factors R B Aird1 again advocated the use of anesthetic gases, especially ethylene for insufflation. He believed that perhaps its anesthetic effects, but especially its speed of absorption, resulted in a lessened immediate reaction to encephalography, minimized the need for supportive, postencephalographic medication, and shortened the period of hospitalization after the procedure from 72 to 30 hours H Newman² on the basis of 30 cases in which he used ethylene, endorsed these claims

Physiology—On the assumption that the injection of gas into the cranial fluid spaces increases intracranial tension, W J McNally, R Scott-Moncrieff, T C Erickson and D L Reeves³ tested

the hearing in 13 cases both before and after encephalography. They demonstrated that encephalography in these cases did not affect the hearing

E D Brewer4 made a study of the mechanism of headache in 86 ventriculography procedures done on 77 patients He found that headache was less severe when ventriculography was done as compared to encephalography In about 42 of his cases there was no headache 17 cases the headache started as soon as the ventricular fluid was removed (5 to 20 cc) and 11 of them were strikingly relieved as soon as the fluid was replaced by air In contrast to this he believed that during encephalography, headache rarely occurred on first removal of the fluid but began only with the first injec-The cases with increased tion of air intracranial pressure most frequently complained of headache after ventriculography The location of the headache was usually in the frontal region and,

since the patients, by the technic employed, were always brow-up during the procedure and the frontal horns were, therefore, first to fill with gas, Brewer concluded that the cause of the headache was mechanical, depending upon an alteration in intraventricular tension

C Bradley⁵ pursued the question of the effect of encephalography on blood sugar levels in children His material consisted of 15 children with "neurologic and behavior disorders" ranging in age from 8 months to 12 years They all had fasting blood sugar levels within normal limits, and all showed hyperglycemia during and after the procedure The rise in blood sugar began during the procedure reached a peak around 200 mgm per cent after an hour, and fell to normal after several hours The curves bore no relation to (1) the anesthetic used, (2) the clinical diagnosis, (3) the patient's (4) the amount of fluid removed or air injected. The cerebrospinal fluid showed no increase in sugar during the procedure

M Scott^o investigated the problem of hyperglycemia in association with encephalography in 75 patients ranging in age from 10 to 62 years. He found that the blood sugar curves tell into three (1) Those in miscellaneous neurological conditions with an average maximum rise to 150 mgm per cent, (2) cases with brain tumor with an average maximum rise to 137 mgm per cent, (3) convulsive disorders with an average maximum of 170 mgm per cent He believed that the relatively low rise in brain tumor cases, and relatively high rise in those with convulsive disorders might be of some significance Scott also demonstrated that the sugar curves following encephalography were not unlike sugar tolerance curves carried out before encephalography in ten of his cases He was led, therefore, to conjecture that the mechanism might be located in the same area As a further link in his reasoning. he called attention to the similarity of symptoms resulting from encephalography to those noted by Cushing after the direct injection into the ventricle of posterior pituitary hormone Cushing was able to control the symptoms he produced by subcutaneous injections of atropine, and Scott also succeeded in ameliorating the post-encephalographic symptoms in this manner He postulated that posterior pituitary hormones may be liberated into the ventricular fluid during encephalography and that this may account for the rise in sugar contents of the blood

Treatment of Symptoms — R S Schwab, J Fine, and W J Mixter,7 on the principle that inhalation of 95 per cent of oxygen accelerates the speed of absorption of air from body tissues and spaces, tested the effect of such inhalation on the reaction to encephalography They reported its use in 37 cases and found in most of them that not only the severity of the symptoms but the cellular reaction in the spinal fluid was diminished Roentgen examination of the skull, after three hours of oxygen inhalation following encephalography, showed the removal of most of the air from the subarachnoid spaces and a marked diminution of the air in the ventricles

They also described a simple apparatus for oxygen inhalation. Their technic was to administer sodium pentobarbital, 4½ to 7½ grains (0.292 to 0.492 Gm) before encephalography which kept the patient asleep during the procedure, and to start the oxygen inhalation as soon as the plates were taken. They believed that the symptoms were further minimized by an intramuscular injection of posterior pituitary extract to increase the secretion of cerebrospinal fluid to

replace the gas, and still further if oxygen was injected instead of air

Encephalographic Anatomy

In a book entitled "The Normal Encephalogram," Davidoff and Dyke8 have collected their experience with 4000 cases as regards technic, indications and contraindications for the performance of the test, and the reaction of the patient during and after the procedure Since they believed that it was extremely important to emphasize a detailed knowledge of the normal intracranial contents as seen in the encephalogram as a basis for diagnosis of pathological conditions by this method, they devoted the body of the book to what might be termed "encephalographic anatomy," describing the individual cerebral structures as outlined by gas in each of the fluid spaces

A E Childe and W Penfield,9 in another of the series of papers on pneumographic studies from the Montreal Clinic, reported upon the anatomy and pneumographic appearance of the temporal horn They called attention to the importance of proper posturing of the patient's head in order to visualize the temporal horns and to the importance of the distortions of these horns in the diagnosis of neighboring tumors. One matter of interest which they pointed out was that the temporal horn may be seriously affected but is seldom obliterated by a neighboring mass. Their explanation of this phenomena was that the choroid plexus, since it extends to the tip of this division of the lateral ventricle, continues to secrete fluid and maintains the patency of the cavity

Diagnosis—W L Holt, Jr, and G B Pearson¹⁰ reported three cases with subdural hematoma in which they found large collections of subdural gas following encephalography In two of these cases the ventricles did not fill at all

They concluded that in cases with a history of head injury, with large collections of gas in the subdural spaces, a subdural hematoma should be suspected.

R Carrillo,¹¹ using lipiodol in the ventricles instead of gas, was able to visualize the hypothalamic portion of the third ventricle with great clarity. He concluded that when the infundibular portion was not visualized, the underlying condition was arachnoiditis in the chiasmal region

A contribution by the Scandinavian radiologist, E Lysholm¹² on the visualization of the third and fourth ventricles consisted chiefly of engravings from roentgenograms beautifully illustrating distortions of these cavities as well as the aqueduct of Sylvius by neighboring tumors

Normal encephalograms in association with clinical signs of increased intracranial pressure accompanied especially by papilledema and failing vision were described by L. M. Davidoff and C. G. Dyke¹³ in a condition which they called *Hypertensive Meningeal Hydrops*. This is a condition variously named "serous meningitis," "pseudo-tumor," "otitic hydrocephalus" and seems to be a sympathetic hypersecretion of cerebrospinal fluid in the presence of infection in the ears or elsewhere in the body

For better localization of tumors of the cerebrum, L H McConnell and A E Childe¹⁴ described a method of tracing a projection of the encephalogram upon a diagrammatic outline of the ventricular system. The portions of the ventricular system were schematically divided and numbered so that distortions in any one region might be referred to by number. A review of 120 cases studied in this manner and eventually verified by operation or necropsy proved that the method was very valuable.

second paper by the same authors¹⁵ consisted of an application of the above scheme with apparent success specifically to the problem of localization of the tumors involving the basal ganglia, lateral ventricles, brain stem and cerebellum

Also from the Montreal Neurological Institute, a paper appeared on agenesis of the corpus callosum by O R Hyndman and W Penfield ¹⁶ This condition, which is clinically undiagnosable, was shown to have a characteristic appearance in the encephalogram in 1934 by Davidoff and Dyke¹⁷ and again by the present authors. This consisted chiefly of the projection of the third ventricle shadow upward past the place normally occupied by corpus callosum.

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POLIOMYELITIS

By IRVING J WOLMAN, M D

Introduction—Infantile paralysis affected 8450 persons in the United States from January 1 to October 16, 1937, a figure exceeded only in recent years by the 9296 cases in 1935 and 13,600 in 1931. These figures from the Public Health Service announcements show that this dread disease is continually prevalent and remains a perpetual threat

Epidemiology—A recent instructive report of the Health Section of the League of Nations¹ points out that poliomyelitis is now being reported from tropical countries which had been considered formerly to be free from the malady. Thus in India, China, the South Sea Islands, Equatorial Africa, and every country of the globe, the native

populations suffer from the disease in its sporadic or epidemic forms

Etiological Agent — Immunological evidence is accumulating which tends to show that there are a number of individual strains of poliomyelitis virus, indistinctly different one from another. For example, both B. F. Howitt² and J. D. Trask, J. R. Paul, A. R. Beebe, and W. J. German have recovered from fatal human cases strains which are highly virulent for monkeys when given intradermally in minute doses, a property not usually observed. These viruses show minor differences from the others in cross protection tests

Pathology—The olfactory bulbs of nasally infected rhesus monkeys develop

inflammatory changes, whereas such lesions are absent when the disease is produced by inoculation elsewhere.³ In this connection, however, the physician should not forget the extensive study of L. W Smith in London and Smith's book on poliomyelitis (Macmillan Co, 1934), who found significant changes in less than one-fourth of a series of 56 olfactory bulbs removed from about 40 fatal cases in the New York City 1931 epidemic

Portal of Entry—The current trend of thought with relation to the pathogenesis and prevention of the disease is based on the theory that the portal of entry is the nose and nasopharynx Further evidence for this is the demonstration of living virus in the nose of two children two weeks after the onset of the disease 4 Once in the nose, the virus penetrates the olfactory nerve endings, ascends the olfactory tract, and then extends through the brain system to the spinal cord From the central nervous system the virus spreads into the body tissues, exciting general defense mechanisms including antibody formation The nerve tissue is left highly resistant to reinfection, whereas the serum neutralizing power may not indicate much immunity

Immunology—The controversy over the significance of neutralizing antibodies in the blood serum still rages, as it has for many years. M. Brodie, A. E. Fischer, and M. Stillerman⁵ present studies on 117 patients from the New York City 1935 epidemic, to show that there is no definite relation between the presence of serum antibodies and resistance to or convalescence from poliomyelitis. The majority of individuals who lacked protective substances in their blood during the first week of the disease failed to develop any in the months following.

In both the experimental and human reports of the disease, one encounters further confirmation that the humoral or serum antibodies are not reliable indicators of body tissue resistance. Sabin and Olitsky⁶ demonstrated that monkeys convalescent from a paralytic attack of poliomyelitis are resistant to reinfection for months before their serum develops protective properties. In contrast, their series of vaccinated monkeys⁷ possessed serum antibodies although still susceptible to nasal infection

Experiments of this sort raise doubts concerning clinical conclusions based on serum neutralization tests in human beings

B F Howitt⁸ found neutralizing substances in the filtered nasal washings of 14 out of 61 individuals examined. Thirty-six of the 61 had similar substances in their blood serum, although no correlation could be made between the presence of positive serum reactions and positive nasal filtrates Her failure to find antiviral substances in the nasal washings of five immunized monkeys are interpreted to mean that the level of antibodies in serum and secretion are not identical, or else that some other factors are at work Nevertheless this important finding suggests a possible mechanism for the protective action of chemicals dropped in the nose

Claus W Jungeblut⁹ presents several papers on the value of vitamin C therapy in experimental poliomyelitis purporting to show that the disease is less severe in experimental animals given treatment with vitamin C. The results are not spectacular

Protection—Armstrong¹⁰ makes an interesting report of the first large field trial of *picric acid alum spray* in the prevention of poliomyelitis in man. The spray consisted of a solution of 0.5 per cent each of picric acid and of sodium

aluminum sulfate in 0.85 per cent saline. This formula was sprayed into the nostrils with an atomizer, every other day for the first week and once weekly thereafter. It is estimated that about two million individuals, of all ages, in Alabama, Tennessee, and Mississippi were sprayed at least once during the 1936 summer epidemic period.

In evaluating the results of this human experiment many statistical difficulties were encountered, apparently, however, satisfactory protection was not attained, for about as many paralyzed cases developed in the sprayed as in the unsprayed group within a selected area near Birmingham where a careful follow-up study was made

Approximately one out of each five individuals complained of unpleasant symptoms following the spray, the most common being headache, nausea, and local irritation. In addition, five cases of urticaria and two of acute nephritis were reported from the three state area.

The conclusion is obvious that this solution, as applied in nasal spray by the general populace is quite ineffectual as a prophylactic, and uncomfortable to boot

Although the pictic acid-alum preparation tailed to fulfill the hopes of its sponsors, the effort to protect susceptibles by the blockade of the intranasal portal of entry has not been abandoned Working with monkeys F W Schultz and L. P. Gebhardt¹¹ discovered that a solution of zinc sultate gave a more effective and lasting protection than did any other of 40 chemicals tried, including alum and pieric acid. Accordingly, these authors recommended a trial of the method of human beings,12 using one per cent zinc sulfate dissolved in normal 07 per cent sodium chloride solution, with one per cent pontocaine added as a local anesthetic

The technic of this maneuver has been elaborated by M M Peet, B H Echols. and H J Richter,13 who insist that the prophylaxis fails unless the olfactory area high in the nose is covered completely An unusually long atomizer having a special tip is needed, so that the solution can be applied under direct vision directly below the cribriform plate The authors recommend the application of 1 cc of protective solution to each side of the nasal olfactory area for three successive days, followed by single sprays at intervals of two weeks Loss of smell lasting one to two weeks is usually noted but is not regarded seriously

During the present summer and fall in Chicago, Toronto, and elsewhere, the zinc sulfate treatment is being administered on a large scale. Follow-up studies will pass judgment on its efficacy and are awaited with great interest by an informed medical and journalistic world. Experience shows already that Peet's procedure is very difficult to carry out with babies and young children in the highly susceptible age period, who can be treated only by atomizer spraying or by simple dropping in of the solution.

A variation of Peet's method is recommended by R S Pentecost, 14 who mjects 0.5 cc of the solution directly onto the olfactory area through olivetipped ureteral catheter tubing, using a svringe, head mirror, and nasal speculum Preliminary spraying of the nose with a mixture of 0.25 per cent *pontocaine* and 0.25 per cent *ephedrine* is required Complete loss of smell for five days results. A single treatment is considered adequate protection

Prognosis—A discouraging prognosis for respiratory paralysis is given by M Bernard Brahdy's¹⁵ most recent follow-up study of respirator-treated patients at the Willard Parker Hospital, New York City

| \ ear | Type of Lesion | Number Treated | Died During Respiratory Treatment | Died After Discharge | Total No | Deaths Per Cent |
|-------------------------|----------------------------|----------------------|-----------------------------------|---------------------------|----------------------|--------------------|
| 1931 1931 1932–33 | Bulbar Spinal Spinal | 12 34 17 63 | 12 16 8 36 | $\frac{10}{\frac{3}{13}}$ | 12 26 11 49 | 100 76 65 |

TABLE I

Analysis of 63 Cases of Respiratory Failure Treated in Respirator

Of 27 patients who regained sufficient respiratory function to be discharged from the hospital, 13 were dead within three years. All but one of these succumbed to respiratory tract disease usually associated with massive atelectasis. Of the 14 individuals still living, seven are badly crippled, five have residual paralysis, and only two are entirely well.

Treatment — One complication of treatment about which every practitioner should be informed, is an occasional reaction to the intramuscular injection of whole blood. Of a group of 1341 children given such injections at the Children's Hospital of Philadelphia, 16 52 showed fever, malaise, and leukocytosis, with swelling, redness and pain at the sites of injection in two to ten days afterward. These symptoms lasted from two to seven days and left no residua. This reaction was traced to the donor's red cells, which were found incompatible with the sera of the recipients.

S R Kelson¹⁷ found that sulfanilanucle was entirely ineffectual in a small group of experimentally inoculated monkeys treated with huge subcutaneous doses of the drug

An exhaustive study of the New York 1935 epidemic has been presented by A E Fischer and M Stillerman ¹⁸ These authors analyzed very carefully 686 admissions to the Willard Parker Hospital from the standpoints of seasonal incidence, age, sex, symptoms, mortality, spinal fluid, etc. The disease showed a

Only 336 per cent of the patients were under five years, and 75 per cent were under ten years. Sixty per cent were males The children under two years of age displayed greater tendency to develop muscular involvement than did the older ones Of 282 patients admitted in the nonparalytic stage, 80 per cent failed to develop paralysis Ten patients had had tonsillectomies within one month prior to onset, which suggests that the virus entered their systems during or shortly after the operating procedure

Treatment consisted of absolute rest in bed, with sedatives when necessary Paralyzed muscles were supported by No convalescent human sand bags serum, whole blood, or horse serum of any kind was administered to any patient in this series Bulbar involvement was actively treated with suction and intravenous infusions, while for respiratory paralysis the Drinker respirator was used with excellent results temperature was found to be the best criterion for the activity of the disease The spinal fluid cell count seemed to have no prognostic value unless the cells numbered over 500 per cubic millimeter In 8 of 12 cases in which the count was above this figure, paralysis either was present or developed shortly. A strongly positive reaction to the Schick test was frequently found early in the disease The mortality rate for the 686 cases,

26 per cent, was the lowest ever recorded in New York City.

The intravenous injection of hypotonic salt solution is enthusiastically recommended by G M Retan 19 Acting on the hypothesis that reduction of central nervous system edema diminishes the severity of the local inflammatory reaction, Retan, during the summer of 1935, treated 57 acute preparalytic cases with hypotonic salt solution injected intravenously The procedure was done on a Bradford bed frame so that a lumbar puncture needle could be inserted and left in the lumbar spine A solution of 0.375 per cent sodium chloride was run in slowly, at the rate of 10 cc per pound of body weight, each hour, for the first three hours, and then at a slightly slower rate for two hours subsequently At half-hour intervals, the nurse in charge would remove the stylette from the lumbar needle and allow 2 to 5 cc to drain slowly. After a three to four hom rest period a second five hour treatment was given and if necessary, a third treatment six hours later. Most patients required several treatments

The results of this technic were apparently very successful. There was not a single death. Ten cases of severe respiratory paralysis survived without complications. Six patients with paralysis of deglutition recovered promptly. A large number of individuals having muscular weaknesses developed no paralysis, although extremities which were paralyzed before the onset of this special treatment showed poor functional recovery.

Retan recommends that this treatment be given to all cases of poliomyelitis as soon as diagnosis has been made. The presence of pulmonary infection, acute nephritis, cardiac weakness, pyuria, colitis, or cerebrospinal fluid block prevents brain dehydration and interferes with satisfactory application of the method

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POLYNEURITIS AND OTHER NEUROLOGIC CONDITIONS

By J C. YASKIN, M D.

Polyneuritis

The etiology of polyneuritis is often uncertain, and the differentiation between the toxic and infectious forms is frequently difficult | I Madsen⁸ reports the cerebrospinal fluid findings in 84 cases of various forms of polyneuritis These included 49 cases of toxic neuritis (alcoholism, lead poisoning and diabetes). 13 cases of infectious neuritis (diphtheria, scarlet fever and acute infection with an unknown type of virus) and 22 cases of the cryptogenic form His findings confirm the observations of Merrit and Fremont-Smith that the cerebrospinal fluid is nearly always normal in the toxic forms of polyneuritis and nearly always shows the albuminocytologic dissociation of Guillain and Barre in the infectious form. In the infectious form the protein is increased, especially during the acute stage of the disease, the spinal fluid tending to become normal rapidly In a few cases with an increase in the cell count, the clinical findings suggested a meningomyelitic complication of the polyneuritis

Pellagra

Retrobulbar Neuritis-The etiological diagnosis of retrobulbar neuritis is usually difficult. The commonest cause 18 multiple sclerosis Among the less frequent causes are a variety of exogenous toxins To these causes M S Lachman9 add the Fine and G avitanimosis of pellagra They have observed three patients suffering from pellagra who had impaired vision due In the first to retrobulbar neuritis of these the retrobulbar neuritis was diagnosed several weeks before signs of pellagra appeared In each case the presence of skin lesions led to the correct

With the present state of diagnosis knowledge of pellagra, one can only speculate about the relationship of the pellagrous syndrome to the visual disturbances The etiology of the disease is still unsettled Since vitamin B2 or G was separated from the antineuritic factor B₁, it has become more and more apparent that even G is a complex of various factors the number and nature of which are not at all understood history in these cases is usually that of chronic alcoholism over many years with the appearance of pellagra-like symptoms after a spree lasting several weeks has been suggested that the important factor in these cases is undernutrition and damage to the alimentary tract from the alcohol, interfering with absorption considering the ocular disturbance associated with pellagra, the problem of the rôle of alcohol becomes more significant in view of the relative frequency of socalled tobacco-alcohol amblyopia association of tobacco with ethyl alcohol in producing injury to the visual fibers 15 constant There has been an increas ing tendency to regard alcohol as an exciting factor in tobacco amblyopia Recently the rôle of chronic alcoholism in peripheral neuritis has ben questioned It does not seem improbable that a relationship such as exists between vitamin B₁ deficiency and the peripheral nervous system may also exist between vitamin B₂ (G) deficiency and the central nervous system, of which the optic nerve is a part, and that in each case the alcoholism plays only an indirect part. Such a quantitative relationship would offer an explanation of the fact that some alcoholic addicts never suffer from amblyopia, while other relatively moderate drinkers suffer serious insult to the visual

fibers. The question arises whether many cases of "alcohol and tobacco" amblyopia are not complicated by a deficiency of vitamin G.

Painful Affections and Motor Paralysis About Head and Face

Painful affections about head and face and motor paralysis resulting from involvement of cranial nerves are so important that even rare cases deserve special consideration

Ophthalmic Herpes Zoster and Total Paralysis of the Oculomotor Nerve—P Nicolau and S Draganesco¹⁰ report the case of a woman aged 52, five days after contusion of the left frontoparietal region, experienced suborbital and ocular neuralgia. On the following day a vesicular eruption appeared in the left frontal region and the left upper evelid. Two days later vesicles appeared on the outer limb of the cornea and the left nasal ala Mydriasis with loss of the light reflex and ptosis accompanied the cruption Paralysis of the third nerve became total four days later. Superficial keratitis with cyclitis occurred after another five days Regression began only atter five weeks, and three months after onset of the illness, slight ptosis of the left lid, slowness of pupillary reaction to light and residual keratitis were still present. The fact that the cerebrospinal fluid showed no albuminocytologic changes indicates that the infectious process was confined strictly to the nerve pathways and that when the meninges were reached immunization had already occurred 1922 Marinesco and Draganesco advanced the theory that the zosterian vesicle is an ectodermal reaction process, due to intradermoepidermal penetration of a filtrable virus and not to trophic disturbances Nuclear and protoplasmic inclusions in the cells removed from the vesicular area and the presence of infiltrative alterations in the subjacent derma and nerve terminals were demonstrated The propagation of the virus along preformed nerve pathways was called odogenesis by Marinesco and Draganesco. whether ascending (neuroprobasis of Levaditi), descending (Foerster) or by diffusion along all cerebrospinal and sympathetic nerve conductors (septineuritis of Nicolau) According to Levaditi. the portal of entry of the zonal virus in the rhinopharynx,, while Marinesco and Draganesco expressed the belief that the infection is cutaneous A local factor. modifications of the physicochemical properties of the skin, probably influences the localization of the infectious process The course of the virus in the case reported was along the frontal nerve to the Gasserian ganglion, thence to the nasal nerve, the ophthalmic ganglion, the long ciliary nerves and the third nerve, via the motor root of this nerve to the ophthalmic ganglion appearance of the eruption in stages is proof that the zonal virus followed preexisting nerve pathways, its propagation being directed by its neurotrophic affinity and by odogenesis

Facial Nerve

Surgical Repair—Sterling Bunnel¹¹ reports several successful repairs of the facial nerve. He states that in Bell's palsy the process by which cold or infection may cause damage to the nerve should be clearly understood in order In reto rationalize the treatment sponse to the trauma from cold or from infection, nerve in its unyielding bony canal so swells that, as in Wolkmann's ischemia, its own circulation is squeezed out and therefore, from the resulting ischemia, necrosis over a length of the nerve results This is usually in the most distal part in the canal, as taste through the chorda tympani is

often saved Decompression should be a sure cure, but to be completely effective it should be immediate. Considering that 80 per cent of the patients recover spontaneously, this routine procedure would result in many unnecessary operations. If signs of recovery are not present in six months, surgical repair is definitely indicated Decompression may be tried at any time and even if late has helped in several reported cases.

If one can determine early whether the case will fall in the 20 per cent in which recovery does not occur, decompression should be performed at once while the damage is being done Duel advised operation if faradic response is absent, as this denotes a severe lesion. In a nerve block, however, the reaction of degeneration produced by stimulation of the muscle. including loss of faradic response, appears only after from four to seven days and is complete in two weeks By this late time the damage to the nerve will have been done Faradic and galvanic response to stimulation of the nerve disappear as early as in three or four days, but even this reaction is too late to serve as a guide for preventive decompression to relieve the ischemia in time Persistence of faradic response and a quick response to galvanic current indicates a mild lesion that will heal. If signs of complete severance of the nerve are present, with reaction of degeneration and rapid and complete atrophy, there is no method of distinguishing between a mere physiologic block and an organic block except waiting

In the treatment of facial palsy emotional expression should be restored by repairing the nerve itself intratemporally or extratemporally instead of resorting to anastomoses with other nerves. This restores the control of the face by the emotional centers of the brain. If repair of the nerve is impossible, recon-

struction of the face by a plastic operation involving the muscle and fascia is indicated Decompression or neurolysis of the facial nerve often restores function. Direct union of severed nerve ends by means of rerouting the nerve is preferable to the use of a free nerve graft when possible, because with it a more perfect degree of regeneration can be expected Free nerve grafts should be used if the gap is too great for rerouting and will give good results The degree of regeneration to be obtained in nerve repair is in direct proportion to the accuracy of the union of the nerve ends. This argues for accurate, aseptic, surgical repair of the nerve in a clean field by suture as against operation in the presence of infection, pus, free blood, open drainage and merely laying the nerve ends together

Tumors of Peripheral Nerves

Tumors of the peripheral nerves are uncommon, occur in various parts of the body, vary in size, are often malignant and are frequently overlooked tumors cause symptoms by pressure on the adjacent structures as when they occur in thoracic and abdominal cavities; by causing pain and other sensory symptoms, and by various motor phenomena. The majority of these tumors occur in individuals suffering from Recklinghausen's disease A P Stout12 describes two classes of primary malignant tumors developing in the peripheral nervesthose of mesoblastic origin and those derived from neuro-epithelium mesoblastic tumors form by far the largest group They can be subdivided on histologic grounds into the uncommon malignant neurofibroma and the common fibrosarcoma The malignant neurofibroma reproduces the simple neurofibroma on a large scale, with the development of atypical cell forms. The

fibrosarcoma is made up of spindle cells, which are arranged in interlacing bundles, and of collagen fibers, which tend to be wrapped about every cell. The striking clinical features include persistent growth, frequency of reappearance after attempted surgical removal and metastasis (in 20 per cent of the cases of fibrosarcoma) Of tumors reported as belonging to the neuroepithelial group only three are acceptable These presented varying histologic features Four other recorded tumors which may have been primary malignant neuro-epithelial growths are discussed but are rejected for lack of proof One of these was probably a metastasis from a primary tumor of the lung Tumors derived from ganglia which happen to be situated within various nerves are not considered primary tumors of the nerves They are referred to briefly, as one pigmented paraganglioma of the ganglion nodosum situated in the vagus nerve is reported in illustration

There are cases of these tumors unassociated with Recklinghausen's disease Twenty-five such cases are reported by E C Cutler and R E Gross 13 The most frequent sites for the neoplasms are the posterior surfaces of the legs, the anterior surfaces of the arms and neck The tumors vary greatly in size and have a marked tendency to cystic degenera-The benign form is easily separated from the nerve trunk, which can

be left intact. The malignant tumor infiltrates and cannot be separated from its nerve. In dealing with the slowly growing neurofibroma, it is justifiable to peel it off from the nerve, but with those showing a more rapid rate of growth a portion of nerve should also be resected. followed by end to end suture of the nerve Operations on sarcoma of the nerve sheaths should be radical, and in the absence of metastases, early amputation of the involved limb gives the best chance of cure Radium or roentgen irradiation of the malignant forms has been almost universally a disappointing procedure

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PSYCHOANALYSIS

By () Spurgeon English, M D

In the Psychoanalytic Review there appears a "Contribution to the Psychogenesis of Migraine" by Frieda Fromm-Reichmann, M D 1 Through psychoanalysis of eight cases of this malady she

had produced cures in five, improvement in two and no improvement in one From analyzing these cases the author gained the impression that they were all patients suffering from unresolved ambivalence

"they could not stand to be aware of their hostility against loved persons, therefore they unconsciously tried to keep this hostility repressed, and finally expressed it by the physical symptoms of migraine" The author further goes on to give examples of hatred and hostility which had remained repressed in the unconscious of her patients for years before it could be released by the analytical situation An attempt is made to explain the mechanism of how such a symptom might result First, the most plausible and experimentally demonstrable theory of migraine by the neuropathologist is presented which is as follows Migraine is (due to sympathetic irritation) produced by spasmodic contraction of the smooth musculature of the cerebral blood vessels According to Gordon and Stone these angiospasms cause in turn ischemia and edema, which irritate the brain as a whole and its centers, and produce by these means the headache, the visual disturbances, the nausea and vomiting and the urine retention

The author then reminds us that the involuntary muscular system responds to unconscious impulses and believes that while the average person feeling conscious hatred against an adversary uses contractions of the voluntary skeletal musculature to express his hostility the migraine patient represses his hostility into the unconscious where it nevertheless expresses itself through contraction of the smooth musculature of certain cerebral blood vessels hostility thereby gets expressed but its effect is turned back upon the hostile one, as so frequently happens in the neurotic who is at the same time punished for his hostile wishes through analysis hostility becomes conscious and can be expressed outwardly without guilt the symptom disappears

From observations on these patients it was felt that one of the important reasons why so much of the hostility had to remain repressed was because they had come from conventional old families of culture, with strong solidarity within the family, and a highly developed family pride This made disagreements and aggressions toward each other very dif-Such emotional expression was taboo and punishable by exclusion, a thing to be feared Four of the patients had unusual refinement of personality so that their sensitive conscience could not bear to realize the destructiveness of their hostility This gave added reason for repression of hostility in their case

Another point discussed was as to why the head was utilized as the site for working out the conflict This seemed to be because they were "rivals of their beloved adversaries or felt resentful in regard to their intellectuality which they unconsciously wanted to destroy or at least feel superior to" One of them was married to a very brilliant and clever but sexually impotent man who would boast of his intelligence, urge the patient to improve her intellectual education and make fun of her lack of brilliancy Every morning that followed a night when her husband had vainly tried to have intercourse with her, or when he boasted of his brilliancy or blamed her for lack of hers she would have an attack of migraine Another patient was a scientist like her husband and tried to make her own work of less importance than his But analysis revealed an intense secret rivalry with him

In short, the author feels the general mechanism to be that migraine patients primarily want to destroy their partner's intelligence and brilliancy which resides in brain and head, as the concrete representative of their mental capacity. This mental mutilation of another not being

permissible they turn the aggression By this means back upon themselves they do to themselves what they secretly wish to do to their rivals, at the same time punishing themselves for their forbidden wishes The author reminds us that this description of what takes place is of course only part of the story, that as in melancholia these patients have introjected the loved and hated object so that hostility, even when turned against the self, succeeds in injuring the incorporated person Eventually ejection of the incorporated object may take place through an attack of voniting or diarrhea

In the Psychoanalytic Quarterly appears an article on "Psychological Factors in Urological Disease" by Karl A Menninger. The author states at the outset that this article is an attempt to investigate the contribution of emotional factors to pathological tissue alteration in the genital apparatus, particularly the prostate

He discusses first impotence and points out how either the psychiatrist or the urologist may see the patient with this symptom. Either may be too local in his examination, i.e., the urologist examines the genitalia and neglects or does not give sufficient importance to an exammation of the emotions. The psychiatrist on the other hand is likely to examme the emotions and neglect or give too little attention to the genitalia Examination by the urologist often reveals congestion and inflammation of the posterior urethra, and tenderness, enlargement and congestion of the prostate This is generally regarded as being due to masturbatory congestion or local infection, or both, resulting in impotence The patient being made anxious by the impotence seeks advice and the urologist through local treatment by massage, irrigation, endoscopy, etc, brings about

improvement in the local inflammatory process and as a result the impotence often disappears. This serves to substantiate the theory that the impotence was due to the local pathology. However the psychiatrists using the psychoanalytic technic have also made some findings in a sufficient number of cases to warrant consideration. While the urologist often makes vague and inexact reference to psychological factors and the psychiatrist makes vague and inexact reference to the organic status, nevertheless data from both specialists must be taken in good faith

Psychoanalysts find that patients suffering from impotence prove upon examination to have a definite psychological need for this inhibition, in spite of their distress about it In other words, they have unconsciously wanted or needed to be impotent to satisfy certain unconscious emotional tensions. It will not lead us too far afield to list some of the specific emotions which, though they exist only in the unconscious, exert a contrary and prohibiting effect upon the sexual function These consist in one or more of the following first, fears, especially of punishment or of injury, second, hostilities toward the loved oblect, third, conflicting loves, particularly parental and homosexual fixations, and fourth, rejection of the masculine (or feminine) rôle with its responsibilities

Associated with and dependent upon these emotions is a great sense of guilt, and experience has shown that the relief of this sense of guilt by any one of several devices will frequently serve to free the patient from his fears and thus from his inhibitions. The psychoanalysts therefore are quite ready to believe that urological treatment frequently cures patients but they ascribe it not to the structural changes effected by the treatment but to the gratification of the need

for suffering always associated with the sense of guilt, for example, guilt over masturbation. In support of this, they point to the fact that devices for relieving anxiety which do not involve any tissue manipulation are also used successfully as treatment, and to the fact, well known to urologists themselves, that some patients seem to erotize and enjoy urological treatments, even though painful. Walder reports the case of a man in whom this erotization of urological treatment went so far that he could even produce an orgasm by passing a sound into the posterior urethra

It certainly does not seem possible to resolve the matter into such naive conclusions as that (1) impotence may result from prostatis, or that (2) prostatitis may result from impotence, because neither proposition would be equivocally supported by the data of either the urologists or the psychiatrists. But both groups would (probably) agree that (3) impotence and prostatitis are frequently found in conjunction

The author then raises the question as to whether all infections of the urinary tract are accidental and defy analysis or whether some of them do not occur as a response to over preoccupation with this part of the body and where the disease serves to allay a strong sense of guilt Examples are given of cases demanding painful manipulations following a "fling" or refusal to co-operate when a case of gonorrhea seems to be getting cured "too soon," i e, before punishment for the sexual transgression has been complete The theory is advanced that it is conceivable that in some instances the emotional factors so alter the physiological processes of a part of the body that a train of pathological results ensues A case of what seemed to be "psychogenic hematuria" is quoted as an example of this, wherein the bleeding was in response to strong unconscious wishes of a feminine nature.

Another case is presented to demonstrate that a conflict may be solved by what the author refers to as "the cooperation of bacterial invasion, which seems to be invited not through behavior but through some compliance on the part of local resistance"

This patient was a man of 35 whose previous life had been uneventful from a psychiatric standpoint. He had been sent to a distant city as a temporary representative of the firm which employed him and took this occasion to enter into a liaison with the wife of an acquaintance with whom he was thrown into contact in his new location and who had shown him some business favors The affair began upon a platonic basis, but when sexual relations were attempted later he was entirely impotent. He was so disturbed by the experience that he left his post of duty and returned to his wife, with whom he found himself to be quite potent, thus relieving his anxiety temporarily.

Later, however, he returned to the city in which he had been stationed and resumed his friendship with the woman he had disappointed. A tentative engagement was made for another night together, but 48 hours prior to the appointment he developed a urethral discharge. He went immediately to a competent urologist who made a diagnosis of nonspecific (staphylococcus) infection of the urethral and prostate and prescribed the customary treatment-irrigation, instillation, prostatic massage.

The patient persisted in this treatment faithfully for six months but the symptoms showed no improvement. There was at times a profuse discharge, at other times almost none. Ulcers and small abscesses formed in the prostate, so that there was for a time bloody urination.

and a bloody discharge. The symptoms did not show any tendency to subside until after instrumentation by the urologist, who found that some adhesions and pus pockets had been formed in the prostatic structure.

Meanwhile the patient was greatly disturbed emotionally, ostensibly because of his impotence. However, the urologist ascribed this to the local pathological condition and urged the patient to disregard it. He consulted another urologist, who concurred in this opinion and also in the diagnosis, but recommended psychotherapy and referred him to a psychoanalyst. Psychoanalytic treatment was advised which the patient accepted and carried through successfully

The analysis revealed many hidden conflicts The affair was unconsciously an aggression against the wife, but the second woman as the wife of another man (mother) aroused guilt and fear within him. Hence anything interfering with sexual function would solve the problems of his guilt and anxiety. The impotence alone hardly sufficed, however, because it was too humiliating. The infection was a more acceptable form of incapacitating pathology, and it more than balanced the sense of guilt a result of the analysis he was not alone cured of the infection but regained his potency as well

Reference is made as to how frequently a urethral discharge with blood serves to satisfy a teminine component in men. To many physicians and urologists it may seem difficult to conceive that men want to be feminine. It is of course usually a deeply repressed tendency in most cases but on the whole a frequent enough phenomenon, observed by those who work psychiatrically with neurotic individuals.

Finally the author deals with the question of capitalisation of infection. This

would be as to whether some individuals can, through their bodily devices and physiological mechanisms, unconsciously control in some way and to some extent the retaining or rejecting of a deliberately acquired infection. Obendorf had reported two cases of gonorrhea, one of which cleared up completely in three weeks and the other which lasted several months until the patient changed urologists. The second urologist gave the same treatment as the first and the patient promptly recovered.

The author cites two cases to illustrate some of his points. The first case seemed to retain his infection of the prostate for many months in order to satisfy certain emotional needs. When through analysis these needs were understood and reduced there was cure suggesting some operative relationship between the psyche and the local and general immunological defenses. This patient showed very strong feminine wishes and his periodic urethral discharge corresponded in many ways to the reaction of women to menstruation.

As the patient's insight grew into the role he was unconsciously playing (in behavior he acted out many feminine traits, even to dressing as a woman on occasion) he remarked, 'Doctor, I don't believe that those bugs disappear merely because you put some chemicals in their vicinity. It may discourage them, but I think something in the individual himself helps to kill them. I don't know how it works, but time after time when I wanted that discharge to come back it came and as soon as I recognized my perverse wish and really renounced it the discharge went away"

A second case reported shows how an urethral infection in another way solved guilt feelings

A last point the author makes is to bring these cases in line with the hypoth-

esis that there is a self destructive impulse in every individual which, hindered or fortified by other elements in the personality achieves its purpose to varying degrees and in various ways Hence these conditions might be referred to as partial suicides or focal self destruction, bearing in mind that these partial suicides are for the sake of personality preservation These focal suicides may be carried out in a conscious deliberate way, as in self-mutilation, in ways which seem accidental or extrinsically necessary, as in certain accidents and operations There is nothing in the theory to make us doubt that these self-destructive tendencies lying as they do, deep within the fabric of the instinctual life may also express themselves without the assistance of the voluntary nervous system and the striated musculature, and are to be seen as well in the death or injury of organs not directly connected with consciousness

Since so much emotion, especially guilt, arises through genital function, the author feels that more attention must be given by physicians to the ideas, conscious and unconscious, associated with this part of the body

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PSYCHONEUROSES

By WILLIAM Y BAKER, M D, and HERBERT A WIGGERS, M D

The relationship of symptom groups of this broad and comprehensive subject has been clearly and competently dealt with by A Myerson¹ an article in which he reduces clinical entities and names to practical, every day words and cases and in terms of energy, fatigue, frustration, strain, etc, "endeavors to reduce chaotic descriptions of neurosis to one of order and developmental significance"

An effort is made to show that the neuroses "bridge the gap between the normal and certain psychotic states" and for the more severe neuroses and those shading into the psychotic states he offers the term "neuropsychoses"

In a similar endeavor to clarify a chaotic state of nomenclature, L T Woolley² gives a profound, brief, but inclusive portrayal of the obsessive ruminative tension states. This entity is synonymous with psychasthenia and the newer term is far more descriptive and practical

In summary he states that this syndrome of behavior tendencies is not specifically related to religion, sex, age, occupation or other environmental factors. Heredity has no direct bearing but may predispose susceptibility

The specific causative factors, he feels, are states of prolonged emotional insecurity determined by actual environmental threats or by dominant figures in the environment These figures and tensions become topically associated with certain objects or situations in the environment and give rise to the phobias and compulsions

E D Bond' in speaking of "The Wish to Fall Ill" emphasizes the advantages of illness as an escape from discomforting and unacceptable environmental and emotional situations, and stresses the importance of inquiry into the emotional burdens of all patients as a means of gaining a broader and more complete etiological prospective

The extreme of the emotional control of the physiological processes is illustrated by J. A Ryle⁴ in a report of "Anorexia Nervosa"

This condition is characterized by a refusal of food to a varying degree, resulting in marked emaciation and asthenia without the presence of psychotic organic manifestations. The basis for the reaction can usually be found in a fear of ridicule and can be carried to the extent of collapse, and death from starvation or deficiency of food essentials. Therapy is simple and successful, but must be rigidly applied. Removal to hospital where full control of patient is possible is essential. Reassurance, tube feeding and re-educative procedures are therapeutic measures recommended.

Bond's viewpoint again is upheld in a survey of the causes of absence from work because of illness, conducted by Thomas M. Ling 5. The study of the sickness benefits resulted in the conclusion that 'psychological factors were tound to be the active precipitants of 80 per cent of the absences."

E Harms' dealing with "The Social Background of Occupational Neuroses" points out the frequently pathological "carry over" of a man's work into his personality. The mournful undertaker, the sea captain who is "lost" when ashore, the physician who can not enjoy society or social contacts because of his scientific interest and worry regarding the health of those about him, are all examples of those in whom gainful activities do not fill their greater needs and markedly interfere with their activities outside working hours.

The fear of failure in "speed up" systems, physical and emotional mal-adaptation to one's employment are also stressed as important factors

A plea is made for a more careful choice of occupation on basis of personal

capacity and need (rather than social pressure or environmental accident) all of which can be attained by prophylactic planning and preparation of the adolescent individual

Somewhat to this end, in the study of the psychiatric trends of medical education by E A Strecker, K E Appel, H D Palmer and F J Braceland, 7 in which the senior class of a medical school was studied in detail, 46 per cent of the students were found to have problems of personality or emotional adjustment needing psychiatric aid

This finding was substantiated by similar studies in undergraduates by H D Palmer and E O Harper 8

Under the title of "The Psychic Factor of Rheumatoid Arthritis" G W Thomas points out that "the emotional components of arthritis have been mentioned in medical writings since the seventh century" He states, "The disease can not be contemplated clinically without gaining a conviction that it is associated with profound psychological depletion" In a study of 31 patients, psychological conflicts and difficulties were found in the greater number and in many, psychic trauma was concurrent with the attacks

H \ Nissen and K A Spencer¹⁰ have made a similar study and approach to arthritis with varied success J L Halliday¹¹ also deals with the functional and psychological phase of this crippling and little understood condition

G E Daniels¹² points out the relationship of prolonged worry, anxiety, shock and depression to exacerbation or precipitation of diabetes mellitus, offering this as a field for study toward a better understanding of the psycho-physiological relationships of endocrine dyscrasias, as well as an aid to the more successful clinical supervision and control of the diabetic

R A McFarland and J. H Huddelson^{1,3} have made pertinent observations and detailed study of the vascular systems in psychoneurotic individuals through records of the blood pressure and pulse variations described as the "Schneider Index."

They conclude, "The Schneider Index, believed to be a reliable measure of cardiovascular efficiency, has revealed a significant degree of unfitness of the circulatory systems of psychoneurotic individuals"

The similarity of the symptoms of anoxemia and the anxiety, confusion, irritability and apprehension of the psychoneurotic is pointed out and anoxemia is offered as a possible etiological factor in the latter condition

This is also expanded and supported by the work of R. A. McFarland and A. L. Barach¹⁴ on "Response of Psychoneurotics to Oxygen Tension Variations." In this study, in 12 per cent oxygen tension, 21 per cent of the neurotics collapsed, no controls collapsed under this tension. In ten per cent oxygen tension, 78 per cent of the neurotics collapsed, 14 per cent of controls collapsed under this tension. In 50 per cent oxygen tension many psychoneurotic symptoms improved.

From these findings the workers suggest that poor oxygen metabolism and madequate vascular systems are common in psychoneurotics and offer it as a basis for some of the pathological manifestations of psychoneuroses

From the standpoint of therapy, J C Yaskin¹⁵ in a comprehensive review of 100 cases of psychoneuroses, their ethological precipitation factors, course, mode of therapy and results obtained, has clearly shown "the importance of comprehensive neuropsychiatric study and need for utilization of various forms of therapeutic approach". He emphasizes

the complexity of the etiological factors and points out that the final results compare favorably with the results of other branches of medicine.

Myerson reports the use of Benzedrine Sulfate in neurotic individuals and feels it is of marked benefit in those cases characterized by fatigue, depression, indecision, doubts and lethargy. This is only as an amelioration agent, having no curative powers. It is not habit forming or harmful in continued use in individuals with normal cardiovascular renal systems. Dosage recommended is from 2.5 to 20 mgms daily, taken usually in two doses in the early morning and at noon. Later administration frequently produces insomnia.

D L Wilbur, A R MacLean and E V Allen¹⁶ report further clinical aspects of the use of Benzedrine in psychoneurotics. They concurred with the above conclusion and found the drug was most efficacious in the exhaustive types of neuroses, next in the depressions and least helpful in those having marked anxiety. When agitation was present it was increased by the drug. These workers recommend the same dosage given above and emphasize the necessity of concurrent psychotherapy of an active type in conjunction with the medication

The analytic approach to the psychoneurotics is covered elsewhere in this survey

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SCHIZOPHRENIA

By Francis J Braceland, M D , and Donald W Hastings, M D $\,$

The research work on schizophrema continues on a large scale. It is noteworthy that most of it is veering toward the organic side even more strongly than before. Almost every large clinic of note both in Europe and in America now has a department in which schizophrenic patients are treated with insulin shock therapy. This was described in the last issue of the Cyclopedia in detail. In the opinion of the authors, Sakel's article jublished in 1934 is still the most important single contribution made on this interesting subject.

The literature is now full of reports from various clinics setting forth their results. They seem to average clinical recovery rate of about 35 per cent and a social recovery rate of about ten per cent of the remainder. It must be admitted that this is far below the original recovery statistics that were published by Sakel which were set at 85 per cent. One must remember, however, that some of this difference could be accounted for by different diagnostic criteria in use in various countries E D Bond and F J Braceland' in an article on Prognosis in Mental Disease call attention to this and note that the report from Burgholzli shows that out of 990 admissions, 375 were diagnosed schizophrenia and only 11 manic depressive Some of these schizophrenics would undoubtedly not have been included under that heading in American hospitals. Cameron and Hoskins³ point out, "It is interesting to note that there is a higher proportion of unfavorable or guarded reports by writers whose series is small, a fact which suggests that experience is an important factor in obtaining the best results from this technique"

The present authors at the time of this writing have concluded treatment in 50 schizophrenic patients by Sakel's method and have noted a clinical recovery rate of 34 per cent plus a social recovery rate of about ten per cent of the remainder. The results were better than this originally but four relapses in one year lowered the figures somewhat

Work with insulin shock therapy has stimulated workers to great activity Noteworthy among the research units is the active group at Worcester State Hospital and they report interesting findings conceining the electrical activity of the brain during hypoglyceniic shock It has been possible for the physicians to forecast clinical recovery and relapse by a study of brain waves from the patient H Hoagland, D E Cameron and M A Rubin 4 Also by the same authors, "The Delta Index of the Electroencephalogram in relation to Insulin Treatment of Schizophrenia "5 These workers have also found a definite "decrease in sugar tolerance, the blood sugar levels after glucose administration attaining higher values and remaining elevated for longer periods than before insulin treatment"

Even if only 35 per cent of the patients are helped, a wonderful advance has been made in the treatment of this dread disease. Bond and Braceland in the article quoted above, made a five year follow up study of several hundred psychotic patients They concluded that only ten per cent of the patients diagnosed dementia praecox had been helped by any other form of treatment or got well spontaneously If the figures were only to include patients who had been ill less than six months the ratio remained practically the same and they reported 11 per cent recoveries This is in marked contrast to the newer forms of therapy and their figures will serve as a base line for other therapeutic methods to be tested against

In 1934, L de Meduna described a treatment of schizophrenia based on production of convulsions Meduna⁶ described the treatment in the American literature in 1936 As did Sakel, Meduna reported a very high recovery rate (90 per cent) in new cases. There are too few reports published by other investigators as yet to be able to confirm or disagree with these statistics Meduna's torm of treatment is not as complicated as the insulin treatment and more cases can be treated in a shorter time. The main complications have been fractures and dislocations caused by the convulsions

Friedman⁷ sums up the procedure about as follows. Many workers have determined that there are changes in the metabolic and chemical processes of schizophrenia. These changes although minimal do indicate that there exists a type of sluggishness as it were in the bodily economy of schizophrenic patients.

This sluggishness may be translated theoretically in terms of lowered metabolic activity of the brain. It is possible to theorize further and state that there may be a functional barrier to facile absorption or assimilation of nutritive elements set up in the brain of such a patient The mental changes resulting from this barrier would become proportionately irreversible as the disease progresses A therapeutic routine directed against this functional barrier before actual irreversible changes have occurred may reinstate the normal nutritive mechanisms thus providing an unblocked pathway for normal mental functions

Theoretically then we may state that the following therapy is in the nature of an irritative or stimulative means to combat this blocking According to de Meduna, the irritative therapy of schizophrenia involves the setting up of a temporary epileptic state by the use of convulsive drugs This is based upon the study of a large number of schizophrenic and epileptic patients and the noteworthy finding of a very infrequent concurrence of the two conditions, in other words, a type of biologic antagon-1sm similar to the one noted between febrile conditions and general paresis Whether or not the actual motor reactions occurring with the treatment are necessary for improvement or remission cannot as yet be stated Among the 110 patients treated by de Meduna, those who reacted readily with convulsions showed the most favorable and the earliest remissive changes

Treatment—The patient is placed on an alkaline diet: 20 grains (1 3 Gm) soda bicarb are given tid, test urine twice weekly for alkalinity, fluid intake 2000 cc per day, no sedation during the treatment

Metrazol (pentamethylenetetrazol), ten per cent aqueous solution, or 25 per

cent camphor in oil. Camphor in oil is given intramuscularly, the initial dose is ½ ounce (16 cc) and the subsequent doses are increased 1 dram (4 cc) per day. When metrazol is used, injections are given every two days starting with 75 minims (5 cc) and subsequent doses are increased 15 minims (1 cc), at each injection.

When camphor in oil is employed and convulsions occur after any given dose the injection is omitted the following day and the next dose is the same as the convulsing dose. If convulsions do not occur after four injections, three or four days are allowed to elapse before the injections are resumed and then with an increase of 1 to 1½ drams (4 to 6 cc.). The maximum dose of camphor is set at 1% ounces (56 cc.). In the case of metrazol, the doses are increased as stated whether or not convulsions occur. Maximum dose is 4½ drams (16 cc.)

When convulsions occur the patient receives the routine care given an epileptic (except for sedatives). In the case of camphor, convulsions occurred 15 minutes to three hours after the injection and as high as six individual convulsions were noted. When metrazol was used only one convulsion occurred and that immediately

When camphor was used, and whether or not convulsions occurred, there was noted what may be called a deleriform or twilight state somewhat similar to that of a person under the influence of alcohol or cannabis. The patient walked around dazed, and hallucinations occurred. They would at times become destructive and aggressive. These reactions to camphor and somewhat less to metrazol remained for as long as ten days after the last injection.

Petit mal types of seizures were frequently observed with metrazol and to a lesser degree with camphor

Contraindications

Meduna: (1) Failing or decompensated heart; (2) any acute febrile condition, (3) menstruation Friedman (4) Severe anemia or cachexia; (5) any abnormality of blood or urinary constituents, (6) previous history of severe cranial injury to unconscious

From a series of 20 cases reported the following results were noted

Fifteen well enough to go home, two rapid relapse and should have had more treatment, two cases slightly improved, three cases unimproved

Not even any suspicious pathologic changes could be detected during the course of the treatment. This agrees with Medina

Meduna states that the treatment should not be interrupted until 15 or 20 convulsions have been obtained regardless of the clinical state of the patient during the course of treatment. Or else, at least three additional convulsions should be obtained after improvement is apparent. He (Meduna) reports 110 cases. Ninety-six per cent improvement during the first year of illness, less than eight per cent show improvement if illness has lasted over three years.

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SPINAL ARACHNOIDITIS

By Robert A. Groff, M D.

The term meningitis serosa circumscripta, commonly called spinal arachnoiditis designates a localized collection of fluid under tension in the pia-arachnoid giving rise to symptoms and signs of pressure depending upon its position in the spinal axis J. S. C Elkington in reviewing the accumulated literature and adding several cases, a total of 41, has given a complete picture of this disease process

Etiology—Infection and trauma are the essential causes No one infection could be isolated Among the infections responsible for the development of spinal arachnoiditis are severe infections of any type,—syphilis, gonorrhea, system infections, typhoid fever, tuberculosis, and meningococcic meningitis

Clinical Features—Males are more commonly affected than females. The patients usually fall in the age group between 40 and 60 years. The mode of onset and the clinical course is variable. The disease process may develop anywhere along the spinal cord or cauda equina. The thoracic region is involved more often than the cervical cord in a ratio of 2.1. The area from T-1 to T-6 is the site of predilection and the lesion is not necessarily confined to one or two segments but may extend over a number of segments.

Two modes of onset are commonly encountered (1) with spontaneous pain, (2) with symptoms of spinal compression. The pain is usually severe, confined to the roots involved and starts on one side, later involving the other side. The pain begins in one or two roots and spreads, to involve additional roots. According to Elkington, motor and sensory signs are added in 53 per cent of cases below a year, 85 per cent

below three years. Stookey on the other hand, implies a prolonged history of nine years. Sphincter disturbances are a late addition to the picture and trophic disturbances practically never occur. The vertebral column is usually rigid and tenderness is demonstrated on palpation

Spinal fluid studies show that the total protein determination is not elevated unless partial or complete block in cerebrospinal fluid dynamics is present. All authors agree that cell counts of the fluid are not increased and the Wassermann reaction is negative.

A complete or partial block to cerebrospinal fluid dynamics, according to Queckenstedt examination may occur but is not a constant finding

Roentgenographic studies after lipiodol injection into the cisterna magna have demonstrated characteristic pictures. In patients with meningitis serosa circumscripta the radio opaque oil collects in globules for some space above the main lesion, giving the appearance reminiscent of a guttering candle, some of the oil passes through. In tumors, the oil is stopped at the site of the lesion in its entirety

Diagnosis—The diagnosis of meningitis serosa circumscripta spinalis can only be made by inference Certain things point toward this possibility but in no way make the diagnosis. The history of definite spinal trauma, of past infections of the subarachnoid space, of syphilis and of root pains more severe than in tumor with a sudden onset, bring this possibility in the realm of diagnostic lesions.

Operative Pathology—Operative descriptions have enriched our knowledge of the process. The dura mater

pulsates defectively and there is a thickened arachnoid band of adhesions to the overlying dura mater, and more often still to the underlying pia Solitary or multiple cysts varying in size, are usually seen. The underlying spinal cord either shows the effects of compression, being shrunken or indented, or there is a definite disturbance of cord vasculature The prognosis is dependent upon the degree of spinal cord damage

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SPINAL EPIDURAL INFECTIONS

By Robert A Groff, MD

Infection may travel to the epidural space in two ways. The first of these is by continuity from infections close to the vertebral column Examples of this may be found in carbuncles of the back, decubitus and perinephric abscess, the infection extending into the epidural space The second process is by metastasis from a more distant focus by way of the blood stream In this method, there is some debate as to whether the intection of the epidural space is secondary to an osteonivelitis of the vertebra or whether the infection originates in the endural space J Browder and R Meyers1 in a paper on epidural infections, give evidence to support the osteomyelitis theory. These authors report seven verified cases. Epidural space infections may be classified as acute, chronic or subacute. For this reason the symptomatology as well as the neurologic picture vary. The clinical picture is remarkably similar in the three forms and the acute process presents a more or less characteristic syndrome

Clinical Features—A positive history of infection in a distant part of the body is usually obtained. In the course of two or three weeks following this infection, the patient complains of a boring pain in the spine. Frequently it is localized in one or two vertebrae. The pain is constant, annoying and throbbing

and is made worse by coughing, sneezing, and sudden movement or jarring of the spine. The overlying vertebra is usually tender. With these symptoms, there are general evidences of infection, headache, malaise, chilly sensations, sweating, temperature of 101° to 104° F, (383° to 40° C) leukocytosis, increase in pulse rate (100) and increase in respiratory rate (24 to 28)

The neurological findings consist of an objective hyperesthesia in the distribution of the affected roots Later, this may spread to involve the entire area below the lesion Hyperesthesia is then replaced by a loss of sensation below the level of the lesion Sensation disappears in the following order,-temperature and pain, deep pain and vibration, and tactile sense A flaccid motor paralysis occurs in the acute lesions whereas a spastic type of paralysis occurs in the chronic forms With onset of paralysis, varying degrees of abdominal distention are encountered and loss of control of the sphincters frequently appears Retention comes first and is often attended by loss of the urge to urinate Later this retention gives way to overflow incontinence Constipation may be bothersome particularly in the chronic cases

Diagnostic lumbar puncture should be done with the following precautions As the needle is introduced toward the thecal space, the needle should be aspirated every few millimeters. Should pus be encountered, the diagnosis is confirmed and the needle withdrawn. If pus is not recovered, the needle enters the spinal canal and fluid is obtained. The Queckenstedt examination usually shows either a complete or partial block. Spinal fluid examinations may show an increase in cells from 50 to 1000 per cmm (polymorphonuclear and lymphocytes) and increase in total protein content. Roentgenograms do not demonstrate vertebral changes in the average case.

Etiology—With but few exceptions the authors state that the causative organism is the staphylococcus, although streptococcus, pneumococcus, typhoid bacillus, and bacillus pyocyaneous have been reported. The distant primary infection has occurred in almost any part of the body. The most frequent types are abscess, respiratory infection, pneumonia, septicemia and bacteremia, and trauma to the spine.

Pathology—The author states that when osteomyelitis of the vertebra is found it is no different from osteomyelitis in other bones. The lamina of the vertebra is most commonly involved but the body the dorsal process or one of the pedicles may be affected. When the spinal epidural space is invaded by the pathologic process, any degree of involvement may be established from an abscess limited only by the confines of the space itself, to a sclerosing granulo-

matous tumor mass All variations between these two extremes have been described In some of the chronic forms, the pathology is not unlike that seen in Hodgkins disease

The spinal cord when involved, presents a combined picture of thrombosis of the vessels, inflammatory response of glia cells and vacuolization of the white substance. The neurocytes themselves, undergo swelling and chromatolysis, and their nuclei become excentrically placed and may entirely disappear.

Diagnosis—As the authors point out, the chief reason for the failure in the diagnosis of spinal epidural abscess is that it is not entertained as a possibility. The history of infection followed by severe boring pain in the back and toxic symptoms, should suggest the diagnosis at once. The neurologic finding of incomplete transverse myelitis is important but by no means indispensable

Treatment—As soon as the diagnosis of spinal epidural abscess is established, *laminectomy* should be done immediately. A wide exposure should be made to permit free drainage. In the chronic form, removal of the granulation tissue may result in opening of the dura and meningitis may follow. For this reason, section of the mass in the middle with the idea of relieving the tension on the spinal cord may be the best treatment.

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SPINAL CORD TRAUMA

By ROBERT A GROFF, M D

Minor Injuries of Cervical Cord

Injuries to the spinal cord with obvious signs present no difficulties in their recognition. This is true when the

history precludes a neck or back injury and the signs presented are without question due to a spinal cord lesion. However, when the patient receives a severe

blow upon the head, too often the signs elicited are attributed to brain damage and the possibility of a spinal cord lesion is not entertained. This has been pointed out by F M. R. Walshe and J Ross1 in a recent paper They state that the types of injury to the head which may produce spinal cord pathology are direct from above blows, such as falling objects hitting the vertex, and pitching body falls in which the head strikes the object on the vertex. Both types are forces transmitted through the long axis of the body and usually produce changes in the cord between C 4-5 or C 5-6 The latter is the common site

Clinical Picture—The patient may complain of a numb feeling from the neck downward or simply a tingling in the arms and legs immediately after the accident Paralysis, if present, is not severe or profoundly disabling During convalescence the patient commonly complains of pain radiating down one or both arms and cold weather tends to make it more severe. A sensation of tingling down the arms may accompany this pain. After resumption of activities, the patient notices a definite weakness in both arms or the arms and legs.

Neurologically these patients show clumsiness in the movements of the fingers indicative of an upper and lower motor neurone lesion. The spinati, deltoid, biceps and triceps muscles may show weakness, and wasting of these muscles may be seen several weeks after the accident. This is variable. The legs may be slightly hypertonic and demonstrate an extensor plantar reflex (Babinski). No sensory changes are found. One patient had a partial Horner's syndrome.

The reflexes are the diagnostic feature in minor cord injuries. The triceps jerks

are greatly exaggerated, the biceps jerks are normal or diminished and the supinator jerks are replaced by finger flexion. It is this differential behavior of the arm reflexes that points to a lesion of the spinal cord in the region of the fifth cervical segment and is termed inversion reflex.

The inversion reflex is usually associated with an increased triceps reflex and a diminished pronator reflex (percussion on head of radius with production of pronation of wrist) It is seen in syringomyelia, traumatic and compression lesions of the cervical cord Three conditions must be present in order to obtain the inversion reflex, (1) a lesion of the fifth cervical segment, (2) an intact eighth cervical segment, (3) the pyramidal tracts must be involved higher than the eighth cervical segment The reflexes in the legs may be exaggerated with an accompanying ankle clonus An extensor plantar reflex (Babınskı) was present in four out of six of the authors' cases The gait is usually slightly spastic The patient trips easily and falls hard, because there is slight weakness in the muscles producing dorsiflexion Bladder symptoms are uncommon Only one patient had incontinence of urine The cervical spine shows limitation of motion and pain is produced at the end of rotation of the head to either side Recovery is extremely slow and imperfect Walshe and Ross state that because there is no sensory change or sphincter disturbance in these patients, the diagnosis may be confused with amyotrophic lateral sclerosis, progressive muscular atrophy or primary lateral sclerosis

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SPINAL CORD TUMORS

By Robert A. Groff, M.D.

Intervertebral Disc

W A Hawk¹ gives a composite picture of the reported cases of tumors of the intervertebral discs together with several cases of his own Up to the time this paper was published only 58 cases had been reported in the literature Since then, a few additional reports bring this figure up to approximately 100

Lesions of the intervertebral disc constitute about five to ten per cent of cord tumors (Hawk) and have been referred to as enchondroma, cartilage nodes, fibrocartilaginous extensions of the disc, enchondrosis and herniation of the nucleus pulposus Whether all protrusions of the intervertebral disc produce symptoms is doubtful. The work of Schnorl, G shows that in a series of 2000 autopsies in which the spinal column was examined 736 presented herniation of the disc into the structure of the vertebra or posterior displacement of the disc under the longitudinal ligament

The tumors are small, measuring from one to two centimeters and microscopically show hyaline cartilage, fibrocartilage, calcified or ossified cartilage tissue resembling the nucleus pulposus or tissue consisting of dense fibrous stroma

Pathology—Two theories have been proposed to explain the pathology. The first considers the protruding tissue neoplastic because of the variation in size and immaturity of the cells, the presence of multinucleated cells and the gradual change of this tissue to normal fibroblasts at its attachment to the disc. The other theory favors hermation of the disc with hyperplastic and fibrocartilaginous changes. Those who support the latter view state that the tumor fails to resemble chondroma because pure

chondromata are usually found during the adolescent period and cease growth with the cessation of body growth

Clinical Features—The average age incidence in 58 cases was 45 years, ranging between 20 and 63 years. Two-thirds of the patients were males and in one-third, a history of trauma was obtained J. S. Barr, A. O. Hampton and W. J. Mixter² in a report of 58 cases with disc tumors in the lumbar region, state that the history of trauma was obtained in 80 per cent of their cases

According to Hawk, the symptoms may be divided into prodromal and initial symptoms. The former consist of "lumbago," sciatics, or pain in the back; the average duration of these symptoms was five years. These sensory symptoms were present in 90 per cent of the reviewed cases, the remaining described some form of paresthesias.

The initial symptoms proper consisted of pain in the back and weakness or stiffness of the legs. The average duration of these symptoms was 18 months. The usual course is first sensory disturbances, then motor and very late sphincter loss.

When the involved disc is located between the lumbar vertebrae, there may be pain radiating unilaterally down the posterior part of the thigh and the posterolateral part of the calf. There may be pain in the buttock or in the lumbosacral or sacroiliac region. Not infrequently, neurological signs are absent.

A complete block in the cerebrospinal fluid dynamics was found in 25 per cent of the cases, and partial block in 50 per cent. Quantitative protein examinations showed a marked increase in 40 per cent and a moderate increase in an additional 40 per cent of the cases. The cell count

In the spinal fluid was always under ten Barr, Hampton and Mixter make a special point of doing the lumbar puncture as low as possible, preferably at the lumbosacral juncture, since so many of these lesions are low in the lumbar region. They further emphasize that protein determination should be done upon the first two to five cc. of fluid obtained, because the protein content is less as more fluid is withdrawn. The increased protein according to these authors is the result of root irritation and not due to block in the cerebrospinal fluid circulation.

Roentgenograms of the spine demonstrated the lesion in seven instances out of 58. The identifying changes were marrowing and irregularities of the disc space and calcification of the lesion. Hawk states that 40 per cent of the 58 cases showed a complete stoppage of lipiodol which was injected into the subarachnoid space.

Barr, Hampton and Mixter show the value of lipiodol injection in the diagnosis of this lesion. The indication for this procedure is an intractable sciatic pain, not influenced by well tried orthopedic measures, an increase in the protem content of the spinal fluid and a block in cerebrospinal fluid circulation This last finding need not necessarily be present. The defect is visualized by fluoroscopic examination on a tilting roentgenoscopic table with the patient's face down, and must be a permanent abnormality, not influenced by rotation or tilting of the patient in any direction Films should be taken to verify the location and the defect. The reviewer wishes to emphasize the fact that the

defect should be verified several times by both downward and upward passage of the oil

The lumbar region is most commonly affected The cervical region comes next, and the thoracic and sacral regions last Considering each region separately, the fourth and fifth cervical, sixth and seventh thoracic, and third and fifth lumbar discs are the sites of predilection

Differential Diagnosis—The following points favor the diagnosis of an intervertebral disc tumor, (1) a history of preceding trauma, (2) intermittent root pains, (3) an initial onset of root pains followed by weakness and late development of sphincter difficulties, (4) demonstration of defect on the anterior canal wall opposite an intervertebral disc by the injection of lipiodol in the subarachnoid space

Prognosis—Lesions located in the lumbar spine offer by far the best outlook Cervical lesions are not as promising, while thoracic disc tumors are least promising of all Obviously the length of the disease picture influences the prognosis

Treatment—The only form of therapy is laminectomy with removal of the nodule Barr, Hampton and Mixter feel that this lesion weakens the spine They plan a small laminectomy, removing only two lamina, the ones above and below the lesion and do a spinal effusion immediately following to give support to patients who do heavy work

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DISEASES OF THE SKIN

By John B Ludy, AB, MD

Lupus Erythematosus

John B Ludy and Edward Corson have noted a definitely high incidence of hematoporphyrin in the urine of cases of lupus erythematosus, especially in the acute disseminated variety. Nearly 47 per cent of the latter and 36 per cent of the chronic form were found to give positive results indicating abnormal quantities of the substance. Whether acute or chronic, activity and progress were noted in the skin lesions at the time of examination when the results were positive.

Among the pathologic states in which hematoporphyrin is reported in the urine, lead poisoning is mentioned As a number of these cases were known to be exposed to lead, usually by reason of occupation, biopsy plugs were incinerated and found to show acute lead retention by spectroscopic examination To combat this influence, various measures, including a metal-free diet, proved helpful to the lupus and later biopsy plugs showed marked diminution or absence of the lead Controls with other skin diseases gave negative tests for lead with the exception of three patients with vitiligo Lupus erythematosus has been observed to be decidedly more prevalent than formerly, the incidence rising to 26 per cent in 1936

Dermatitis Probably Due to Motor Fumes

Arthur Whitfield¹ reports a case of dermatitis of the face occurring in a woman who had been driving in a closed automobile. On changing to an open car, the dermatitis entirely disappeared and has not recurred. He suspects the sensitizing substance may be acrolein, derived

from the imperfect combustion of lubricating oils

Aniline Dyes in Treatment

M Bruckner² cites his experience of the value of one per cent brilliant green in alcoholic solution, Castellani's fuchsin paint, and the Greifwald Eye-Clinic mixture. Their relative value varied somewhat according to the cases treated, but, taken as a whole, the Greifwald Eye-Clinic mixture has given the most satisfactory results, particularly in superficial pyodermias, epidermophytosis, intertrigo, seborrheic and impetiginous eczema. The formula follows

| Brilliant green | 1 | 1000 |
|-------------------|---|------|
| Hoffmann's violet | 1 | 1000 |
| Malachite green | 1 | 1000 |
| Methyl violet | 1 | 1000 |
| Safranın | 1 | 500 |
| Magdala red | 1 | 500 |
| Toluidine blue | 1 | 500 |
| | | |

SCHÜLLER-CHRISTIAN'S DISEASE

T R B Atkinson; describes this very rare disease which is characterized by defects in the bones (usually lacunar osteoporosis of the skull), exophthalmos, diabetes insipidus, and arrest of skeletal growth

Certain skin manifestations have been reported to be present in this affection. Hand found the skin to be dry and scalv. Hofer describes a dry scaly eruption of the scalp and papules occurring on the anterior surface of the trunk, Herzau and Pincus noted an elephantiasis of the penis which occurred in this disease (the only one reported in literature)

It is generally agreed that this disease results from a disorder of the lipoids, but

xanthomatosis of the skin has not been described as being present. The disease is not hereditary. Males are affected more than females and it commonly occurs between the ages of two and eight.

Virus Diseases of the Skin

Case of Kaposi's Varicelliform Eruption⁴—During 1937 two cases of Kaposi's varicelliform eruption occurring in adults were reported in Philadelphia One occurred in the Lankenau Hospital and the other occurred in private practice. In 1936, two cases of this rare disease were reported occurring in babyhood, one at the Mary Drevel Home, and the other in the Philadelphia General Hospital. An abstract of a paper on this disease is therefore doubly interesting.

R T Brain and Beatrice Lewis believe that Kaposi's varicelliform eruption has many clinical features of an acute virus infection and recent work suggests that the vaccinia virus is the etiological agent

Kaposi's varicelliform eruption presents a clinical picture which is indistinguishable from generalized vaccinia, and when such an eruption is an immediate sequel to vaccination, the diagnosis of generalized vaccinia is rarely in doubt.

On the other hand, when a patient with a pre-existing skin disease, usually intantile eczema or Besnier's prungo, develops such a papulo-pustular eruption with no history of recent vaccination or of contact with vaccinia, the disease is labelled "Kaposi's varicelliform eruption"

In spite of the clinical resemblance to generalized vaccinia, the disease can not be ascribed to that virus, nor has any definite evidence been obtained to support or negate its relationship to vaccinia

Since Kaposi's original description in 1887, similar cases have been reported

by Juliusberg (1898), Baar and Freud (1931), Feit (1933), Brown and Mc-Lachlan (1934), Goeckelman and Wilhelm (1935), Corson and Ludy (1935), and an epidemic in Glasgow was reported by McLachlan and Gillespie in 1936. Few attempts have been made to establish a virus as the causal agent.

The Glasgow epidemic described by McLachlan and Gillespie was not investigated from the virus aspect, but from bacteriological studies evidence was submitted for regarding streptococci as the possible causal agent. However, McLachlan and Gillespie admitted that the clinical appearance and histology were more suggestive of a virus infection.

The following is a report of a case of Kaposi's varicelliform eruption first seen on November 3, 1936

The patient, E R—, was a schoolboy, aged 15 years. He was vaccinated when three months old, and a week later developed eczema, which persisted as Besnier's prurigo with considerable xerodermia. Between the age of 18 months and tour years he had occasional attacks of asthma, and ran the usual relapsing course characteristic of the "prurigo-eczema-asthma syndrome". He was an only child, his grandtather had asthma, one uncle had asthma and migraine, and another uncle had had eczema as an intant.

Before the present illness the boy felt tired and worried by school examinations eczema had been more troublesome and the cervical glands became swollen and painful, as they had been on some previous occasions His appetite was good, and he was gaining weight His mother reported that on the evening of October 31, 1936, he felt tired and went to bed with slight pyrexia On the morning of November 1 his temperature was 103° F, and his skin began to look inflamed and spotty over his arms, neck and forehead His head and eyes ached, he felt ill and sick, but apart from the swollen glands in his neck he felt no actual pain. His temperature steadily rose to 104 to 105° F (40 to 405° C) On November 2 the skin-lesions, as described by the local doctor, were evidently papules and pustules, with some umbilication, and these lesions were increasing in number. His temperature remained high The patient had not been vaccinated since infancy, and the most searching inquiry revealed no history of contact with either a case of vaccination or a recently vaccinated person sparse on the upper part of the chest and back, and on the flexor aspects of the arms, the rest of the trunk and limbs being free He had a thickly furred tongue, marked enlargement of his cervical and avillary glands



Fig 1—Kaposi's Varicelliform Eruption—Lesions, which consist of umbilicated vesicles and pustules with secondary crust formation, occurring on the thigh of a patient with Kaposi's Varicelliform Eruption (Ludy)

When first seen on November 3 the patient had a temperature of 104° F, and merely complained that his skin felt stiff. Scattered over his face, almost confluent on the forehead and neck, were umbilicated papulo-pustules completely suggestive of vaccinia. The lesions were

The spleen was not palpable. He was admitted to the Royal Free Hospital the following day. On admission his temperature was 100.2° F, pulse 76 and respirations 20. He was pale, and looked ill and toxic. The eruption was as described, but more lesions had appeared on

the arms, and many of the lessons on the face had become confluent

Progress—The patient ran an irregular temperature, varying from 99 to 1045° F (372 to 403 C), pulse-rate from 76 at onset to 124 in the latter few days, and respirations from 20 to 40 Pustulation was progressive, and the whole of the face, neck and forearms were largely scabbed and purulent with considerable



Fig. 2 (case 3)—I estons on the day after the patient's admission, the sixth day of the case ise. Crusting has progressed to a point where many or the umbilications are oblitcrated. This tenture especially on the torehead can still be made out with a reading glass. (American Journal of Diseases of Children December 1935.)

ordena (The photograph shows these teatures very well). His cyclids were swollen and painful and a purulent conjunctivitis was troublesome but the cornea was not involved. It is purpuric spots appeared on his knees and ankles from November 6 to 12, 1936. On November 8 the scabs began to separate, leaving extensive raw areas. His throat was painful, and many vesicles were seen on the tongue and buccal mucosa. November 10. Raw areas of skin present over face, back of neck and forearms. Patient's general condition deteriorating. Temperature reached 100.5° F (381° C.), pulse 110, and respirations 24. A haemorrhagic diarrhoea developed. November

12 Diarrhoea persisting, but no longer haemorrhagic Patient drowsy and delirious at times Temperature 104° F (40° C), pulse 114, respirations 34 Areas of consolidation present in both lungs suggested broncho-pneumonia Patient's general condition continued to fail with increasing delirium, and he died on November 15, 1936

The patient's general treatment was mainly symptomatic, but at first he was put on quinine, gr 11J, aspirin, gr v, 4-hourly, and, later, colsulphanyde

The following investigations were made

- 1 Blood-culture put up on November 5, 1936, remained sterile
- 2 Cultures from numerous skin-lesions were made New vesicles on the chest-wall yielded staphylococcus pyogenes aureus only New and old vesicles, pustules and crusts from the face, arms and fingers gave S pyogenes aureus and a haemolytic streptococcus of the pyogenes type, which gave a positive Group A precipitin test (Lancefield), but was untypeable with Griffith's sera
- 3 Cultures from throat, nose and a lesion inside the lip Haemolytic streptococci present, belonging to Group A, but not typeable
- 4 Blood-count Haemoglobin, 76 per cent, red blood-cells, 4,970,000 per cmm, color index, 0.75, white blood-cells, 11,000 per cmm, lymphocytes, 19 per cent, polymorphs, 78 per cent, monocytes, 2.5 per cent, eosinophils, 0.5 per cent
- 5 Specimen of stool Fluid, offensive, bright orange color, red blood-cells and few pus-cells present

Film Numerous gram-positive and gramnegative bacilli, and relatively increased number of streptococci

Culture B coli, non-haemolytic strepto-cocci, gram-positive anaerobic bacilli

- 6 Auto-inoculation on November 7, 1936 The cheesy contents of an umbilicated unbroken vesicle were rubbed over a scarified area of skin, 1 cm across, on the front of the chest, and covered with a watch-glass and strapping No lesion developed
- 7 Histological preparations from an umbilicated pustule on the wrist were searched for inclusion bodies, but none were found
- 8 Animal inoculations (a) Guinea-pigs On November 5, 1936, vesicle-tops and crusts were taken from the patient's skin, emulsified in saline and left in the cold for 36 hours. The centrifuged fluid was inoculated intradermally into plantar skin of guinea-pigs. In

two days lines of pus were visible, and by four days the pads were distended with pus, from which haemolytic streptococci and staphylococcus aureus could be cultured Material taken from the patient on November 11 gave no reaction in guinea-pigs' pads, and no other positive results could be obtained on repeated inoculation of guinea-pigs, either with ante-mortem or post-mortem material from the patient, or with rabbit material

The pus obtained from the (b) Rabbits guinea-pigs' pads was inoculated into the scarified cornea of a rabbit. For four days the eve looked normal On the fifth day there was slight injection of the blood-vessels, with a tiny bead of pus at the inner canthus By the seventh day there was an intense purulent conjunctivitis, and a visible irregularity of the cornea on the inoculated side only The animal was killed and the eye enucleated for histologi-Pus from the eye was used to cal study moculate the scarified cornea of a second rabbit A positive reaction began on the fourth day and was intense by the sixth day By passage five rabbits in all gave positive reactions in the form a kerato-conjunctivitis Further attempts at passage were unsuccessful From the second rabbit onwards the conjunctival pus yielded on culture staphylococcus albus only, of which live one-day-old cultures tailed to produce a reaction on scarified rabbits' corneae Sections of the affected corneae and films of conjunctival pus were examined for inclusion bodies, but these could not be demonstrated Attempts to produce skin and testicular lesions in rabbits were made with post-mortem skin material from the patient reactions suggested positive Inflammatory 'takes" but attempts at passage were negative, which made the findings inconclusive corneal nor conjunctival reaction was obtained by control inoculations of rabbits' corneae with live pure cultures of streptococci or with staphylococci isolated from this patient, or from other patients with septic skin-lesions

9 Serological tests One of the rabbits with an intense kerato-conjunctivitis was allowed to recover, and showed much corneal scarring of the affected eye. Dr. M. Salaman, of the Lister Institute, kindly carried out tests on the serum of this rabbit for agglutinins, precipitins and neutralizing power against vaccinia virus. All the tests were negative. A normal rabbit was inoculated intratesticularly with an emulsion of crusts from a skin-lesion taken from the patient at post-mortem.

was an intense testicular reaction, which could not be propagated to other rabbits. An emulsion of the affected testicle was injected intravenously into a rabbit, whose serum was subsequently tested by Dr. Salaman for evidence of infection with vaccinia virus, but again the results were negative. Post-mortem material, particularly when obtained late in disease, is very unsatisfactory for investigation, and in view of this fact, no conclusions can be drawn from the negative findings here reported.

Lipstick Dermatitis

F F. Hellier⁵ considers lipstick dermatitis a well recognized though somewhat uncommon condition.

The clinical picture of lipstick dermatitis is very characteristic. Varying from two to twenty-four hours after the application of the lipstick, the patient experiences an intense itching of the lips which may be actually painful and the lips become swollen and puffy looking, and in some cases are even covered with vesicles. If no further lipstick is applied the condition clears up in a shorter or longer period up to ten days, according to the severity of the attack. This process is associated with desquamation from the lips

Sometimes the attack is so severe that the itching and erythema spread beyond the lips to the cheeks. Occasionally the tip of the tongue is affected and rarely the application may be accidentally carried to the patient's eye

As in other forms of sensitization dermatitis, the condition may occur on a first contact with the lipstick, but frequently it results from a lipstick which the patient has been accustomed to use over a period of years

It might be confused with a dermatitis from some other irritant such as a tooth paste, but the history will make the diagnosis obvious

Lipsticks vary in formula but have in general three groups of constituents

forming respectively the base, the perfume and the color

The base consists of a mixture of waxes, alcohols, oils and fatty acids. The following is a typical formula

Beeswax 24, Paraffin 6, Stearic acid 6, Cetyl alcohol 4; Spermaceti 8, Lanolin 9, Lard 32; Cocoa butter 8, Oil ricini enough to make 100

The above base is rarely the cause of lipstick dermatitis, however, landlin and ceresin occasionally may produce a dermatitis

It is probable that various prefumes may act as irritants, but in these cases the patient often cures herself by a change of lipstick

The colouring matter appears to be the most frequent cause of irritation

The majority of lipsticks contain eosin and by far the greater number of dermatitis cases have been due to eosin

If lipstick dermatitis should occur in summer rather than in winter, it is probably due to dives which are powerful photosensitizers. Two of these dives, Bordeaux red and chodamine B, should therefore be discarded in the making of lipsticks.

Roentgen Ray Ulcers

Leaf of Aloe Vera in Treatment— Adolph B. Loveman⁶ describes the technic of application of both the fresh whole leaf and an outment containing the intestinal contents of the leaf

Viv one who has seen the horrible suffering endured by patients with some of the late sequelae of roentgen and radium irradiation and who realizes the utter futility of previous methods of treatment will welcome any suggestions which offer relief of these symptoms

The author reports two cases

In the first case there was no relief from pain for two or three weeks after the fresh whole leaf was used He states that this is unusual, as a rule, relief follows two or three days of treatment

In the second case, although the pain had been so severe as to require opiates, it had almost entirely subsided 48 hours after the leaf had been applied to the affected area

In the first case the onset of healing was not noted until the leaf had been used for about six weeks

In the second case epithelization was noted in 48 hours, although the ulcer did not completely heal for three months

The duration of the roentgen ray or radium ulcer is important from the stand-point of prognosis. In the two cases reported, the pain disappeared and healing occurred much sooner in the ulcer which had been present the shorter period of time. The author feels that treatment should be continued with the fresh whole leaf for at least from three to nine months before the treatment is discontinued.

Styes

Treatment — Harry Leonard Baer and Joseph M Shelton⁷ state that infections occurring about the hair follicles of the eyelids and producing blepharitis or localized abscesses (styes) are at times recalcitrant to treatment Recurrences are frequent, and attempts to elicit such possible etiologic factors as error of refraction, metabolic abnormalities and focal infections have been of no avail

The following prescription they state has been used successfully for many years at the McCoimick Hospital in Siam, where blepharitis is prevalent among the natives

Rydrarg oxid flav 11 grains (0 13 Gm) Ol ricini (tasteless) 4 minims (0 246 cc)

Petrolatum alba 511 (39 Gm)

Sig The ointment is applied with an applicator four times daily

It is believed that the castor oil enhances the chemotherapeutic effect of the yellow oxide of mercury

Boric Acid-Starch Poultice

Douglass W. Montgomery⁸ believes that in prelisterian medicine, poultices occupied a too prominent place and their subsequent neglect has been partly a reversion from this excess

J. M H MacLeod,⁹ in his book, places directions for making the poultice at the head of his list of remedies

The following is the best procedure Mix together in a small dish, one table-spoonful of ordinary laundry starch and one heaping tablespoonful of boric acid powder. Make a paste of this mixture by adding two tablespoonfuls of cold water. Then add to this paste, while constantly stirring, half a standard measuring cupful of boiling water. There are many kinds of starch, but as they do not hydrolyze alike, not all of them make good poultices. A starch made from corn is the best variety

Hydrolyzed starch jells readily and may be applied hot or cold

The under marginal surface of the poultice should be greased with olive oil or vaseline, this will prevent sticking of poultice and facilitate its removal

To prevent the poultice from drying too quickly, a little glycerine may be added to the water used in making it. The poultice should be covered with cellophane or oiled silk.

Scabies

Treatment With the So-called Danish Method—This is a report¹⁰ on 4522 cases of scables in which the so-called Danish method of treatment was used. In 93.85 per cent of the cases, cure resulted from a single application of the ointment. In 5.6 per cent, a dermatitis followed its use.

The ointment used in the so-called Danish method originated in Copenhagen in 1911. Its use was introduced at the Massachusetts General Hospital in 1923, and it has been used at that hospital ever since its first introduction.

Routine for 24-hour treatment.

Printed directions are given; they are as follows:

"This disease is very contagious

"All the members of the family who itch or who have slept with a patient who itches must be treated at the same time if the family wish to secure a permanent cure and prevent reinfections

"Treat as follows

"All take a good hot bath, using soap and scrubbing the body all over carefully with a small brush or coarse wash cloth

"After the bath apply to the body from chin to toes, back and front, the ointment given to you by the doctor Hard rubbing is not necessary. Do not rub ointment on face or scalp

"Leave the treatment on for 24 hours Then take a corn-starch bath and put on freshly boiled and pressed underclothing

"Take all your soiled clothing, including night clothes and underclothing, as well as sheets, pillow cases and towels, put them into a boiler or large pan on the stove and cook for 20 minutes. Press twice with a hot iron everything which comes in contact with the skin and cannot be boiled, especially gloves and stockings.

"Return to the hospital or consult your doctor or nurse in two weeks and they will tell you if you are cured

'Do not use the outment after the 24 hours without consulting your doctor"

Danish ointment is made as follows 11 Make a stock solution of potassium polysulphides by "dissolving" 100 (mi sulfur in 200 (mi of the solution potass hydroxide 50 per cent. Filter

Mix 22.5 Gm petrolatum and 22.5 Gm wool fat. To this mixture add and incorporate 37.5 Gm of the solution of polysulphides. The incorporate fresh zinc hydroxide is prepared as follows.

28 Gm zinc sulfate in solution is added to 4 (im solution sodium hydrox-

ide. 20 per cent Precipitation is washed free of sulphates and allowed to drain Lastly add 0.5 Gm. benzaldehydl and sufficient liquid petrolatum to make 100 Gm

Patients should be warned that there is an intense burning and stinging sensation for five to ten minutes following application of ointment and that there is no danger to the child or baby.

Seroresistant Syphilis

Drs Joseph Earle Moore and Paul Padget, 12 of the Syphilis Division of the Medical Clinic, Johns Hopkins Hospital, Baltimore, ably discuss this unfortunate problem

Patients with early syphilis (infection of less than two years' duration) are considered to be seroresistant if the result of serologic test for syphilis remains positive after six months of continuous treatment, whereas those who present themselves late (after having been infected with syphilis for more than two years) are considered to mainfest sero-resistance only if the result of the reaction to the scrological test for syphilis is positive after the equivalent of a year of treatment

The following questions arising in the mind of the investigator are very important. Does seroresistance indicate persistent foci of spirochetes or progressive syphilitic lesions? Or is the persistence of a reagin in the circulating blood following antisyphilitic therapy simply a manifestation of persistent immunity?

The authors state that no certain answer to these questions is possible because of lack of definitive evidence, either clinical or experimental, but available information indicates that while either or both factors may operate in the individual case, a few generalizations are possible

In the interests of the patient, seroresistance in cases of early syphilis must, on the basis of present knowledge, be regarded as a manifestation of persistent foci of organisms or progressive activity In cases of late syphilis, seroresistance may result entirely from a well established immunity

The incidence of seroresistance varies from about ten per cent in patients with early syphilis to approximately 75 per cent in those who first come under treatment with dementia paralytica

In cases of early *syphilis*, two other factors are of extreme importance in determining the incidence of seroresistance, first, the system of treatment employed, and second, the presence or absence of involvement of the neuraxis

Eleven per cent of patients who receive continuous treatment are seroresistant, while 37 per cent of those treated intermittently and 68 per cent of those whose therapy is irregular give positive reaction to serologic tests more than six months after the institution of treatment

Seroresistance is encountered in only a sixth of the patients whose cerebrospinal fluid is normal or falls in that group where cerebrospinal fluid observations are normal and cells number six or Seroresistance does, however. more occur in almost a fourth of those cases whose cerebrospinal fluid shows an increased protein and the cells number five or more Seroresistance also occurs in half of those cases whose cerebrospinal changes are characterized by positive Wassermann with larger amounts of fluid (from 04 to 10 cc) or showing a tabetic colloidal curve

In patients with late *syphilis*, the situation is entirely different. Seroresistance is a usual or expected eventuality with many forms of late syphilis. Studies from the Medical Clinic of the Johns Hopkins Hospital have shown that the incidence of seroresistance is not influenced by the scheme of treatment employed or related

to the existence of involvement of the In short, it may be neuraxis per se viewed as an integral part of the manifestation of many late forms of the disease In patients with certain types of late syphilis, seroresistance may actually be beneficial rather than harmful

The prolongation of the usual system of continuous treatment to two full years, with periodic observation during the patient's lifetime, will accomplish the desired result of maintenance of good health of patients (probably 95 per cent) with seroresistant late syphilis

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STOMACH AND INTESTINES

Edited by HENRY L BOCKUS, BS, MD

IILCERATIVE COLITIS

By J WARREN HUNDLEY, M D

Diagnosis - Recent contributions to the literature on idiopathic ulcerative colitis have added little of practical value regarding the diagnosis of this condition, although many articles have appeared dealing with the possible etiological factors, bacteriologic and otherwise The endoscopic picture by means of rectosigmoidoscopy and the characteristic x-ray findings with the double contrast barium enema study, still constitute the accepted methods by which the criteria for diagnosis are established. aside from the clinical history

J L Jelks,1 in discussing two different forms of ulcerative colitis caused by streptococci and the Vincent's organism respectively, points out that various strains of streptococci were isolated from the lower bowel, which organisms were also found in his series of patients in foci of infection elsewhere in the body The types of streptococci most frequently encountered included viridans, hemolytic, nonhemolytic and Bargen's diplostreptococcus In his opinion, it was of the utmost importance that these various foci of infection be eradicated Vincent's type of ulcerative colitis, he feels, is frequently overlooked and he emphasizes that a thorough search for the Vincent's organism should be made in every instance in which the rectosigmoidoscopic findings are somewhat atypical. He points out that, unless the Vincent's infection of the mouth or throat, in these instances, is eliminated. the ulcerative colitis will remain refractory to other measures of therapy

In an effort to establish the possible relationship of a virus to the etiology of nonspecific ulcerative colitis, Moses Paulson2 studied a group of patients with ulcerative colitis of undetermined etiology, in whom the presence of a virus in the colon might be related to the colitis, as suggested by their having a positive intradermal response to inactivated bubo pus due to the virus of venereal lymphogranuloma (lymphopathia venerea) (Frei reaction and Frei In attempting antigen, respectively) this study, it was hypothesized that if antigens could be prepared from the bowel material from patients with ulcerative colitis which would give reactions comparable with known positive and negative reactions to Frei antigen, a positive intradermal response with the bowel antigen would indicate the presence of a specific antigenic substance, either the virus of venercal lymphogranuloma of an associated productnonspecific or otherwise, but acting in a specific manner in the intestinal contents from which the antigen was made It was recognized, however, that a positive reaction to the Frei test, associated with otherwise unexplained ulcerative colitis, does not of itself prove that the virus of venereal lymphogranuloma is enologically related to the colitis, it is concervable that a colitis might not bear any relation to antecedent, simple, uncomplicated and healed venereal lymphogranulona or to coinciding venereal lymphogranuloma Experimental and clinical evidence obtained by Paulson's however, strongly studies such a relationship and by further tests with this antigen he hopes to narrow further the classification of nonspecific ulcerative colitis, the cases in which there are indications of the virus of venereal lymphogranuloma in the intestine being separated from those in which there are not, suggesting differences in clinical approach The accuracy of the test as a diagnostic method in indicating the presence of virus in the bowel was based on experience with 409 intradermal tests with 24 antigens on 58 persons

In discussing the bacteriologic aspects of ulcerative colitis, W Z Fradkin³ takes the stand that a case of ulcerative colitis is amebic or bacterial in origin. unless proven otherwise In his opinion, a definite agglutination with Shiga or Sonne dysentery strains in dilutions of 1 40 or higher should be considered diagnostic With the Flexner, Hiss and Mt Desert strains, an agglutination of 1 160 should be required for a positive diagnosis Furthermore, repeated agglutination tests showing a definite rise in the titer of the patient's serum was considered of even greater value in establishing the final diagnosis

As a result of his investigations, Fradkin listed the following conclusions

- 1 An effort should be made to determine the etiology of any case of ulcerative colitis as early as possible
- 2 Material for bacteriologic study preferably should be obtained by aspirating exudate directly from the lesion through the sigmoidoscope
- 3 Specimens must be examined and cultured repeatedly if previous findings are negative
- 4 No medication should be given for at least 72 hours prior to cultural studies
- 5 Intensive investigation of 36 cases of ulcerative colitis, acute and chronic, revealed the Endameba histolytica and the dysentery bacillus as the most common etiological agents. Next in frequency was the diplostreptococcus of Bargen
- 6 Progress in the etiology of ulcerative colitis will depend upon the close co-operation between the clinician and the laboratory staff
- G M Dack, L R Dragstedt and T E Heinz,⁴ upon repeated bacterio-

logical studies in cases of chronic ilcerative colitis, have almost invariably succeeded in isolating the Bacterium necrophorum This organism is similar. if not identical, they believe, to what is called in the literature, especially by the French bacteriologists, "Bacillus funduliformis" From their studies it is quite apparent that Bacterium necrophorum is common in the intestine of man and monkey When the bowel is ulcerated either from a cause unknown or by specific agents such as Endameba histolytica or dysentery bacilli, these organ-18ms find conditions favorable for rapid multiplication In one case the authors showed that when the bowel healed no Bacterium necrophorum organisms were found, whereas the organism persisted in the colons that remained diseased

The fact that it predominates over all other organisms in the isolated diseased colons of patients with chronic ulcerative colitis upon whom ileostomies have been performed, in the author's opinion, is further evidence that it is of etiological significance in this disease. It has not been recovered when the bowel heals. They have failed in several attempts to ulcerate the normal isolated colon of a thesus monkey with cultures of Bacterium necrophorum introduced into the healthy bowel segment. This is in keeping, they state, with what they know of the normal habitat of the organism.

Treatment — In summarizing the present status of treatment in chronic idiopathic ulcerative colitis, J. A. Bargen concludes that therapy in this condition readily divides itself into (1) Rest and restful recreation; (2) diet, (3) serum and vaccines; (4) nursing care, (5) drugs; (6) transfusions, (7) supportive measures; (8) rectal instillations; (9) removal of foci of infection.

F Gallart Mones and P Domingo Sanjuan⁶ reviewed the different therapeutic measures proposed and used in chronic ulcerative colitis, and were skeptical of the results of treatment sults with irrigations were discouraging Mechanical cleansing with physiologic saline solution seemed helpful Mediocre results followed the administration of Bargen's serum and vaccines. They did not observe any local improvement as a result of Rachwolsky's treatment with blood transfusions They tried the administration of tincture of iodine, autohemotherapy proposed Bensaude, the administration of calcium and parathyroid extract advised by Haskell, and the Kalk treatment. The best results were obtained with the administration of reduced iron (2 to 4 Gm a day), and with the administration of opium over a long period of time An adequate diet which was high in calories and vitamins and low in The work cellulose was advised these authors indicates that the damage in chronic ulcerative colitis is done by a filterable virus in association with the streptococcus

In a preliminary report on artificial fever therapy in the management of chronic ulcerative colitis, L K Fergu-Schnabel⁷ Fetter and T G were enthusiastic about the results obtained in all of five patients so treated Their decision to attempt this type of therapy was prompted by the recognition by the authors, as well as by many other observers, of the fact that any therapeutic procedures which were associated with the production of a fever gave the best results in ulcerative colitis Thus, in the use of vaccines or sera, a therapeutic effect has been noted in proportion to the reaction which followed the injection of these foreign proteins Likewise, blood transfusions which have

been followed by a posttransfusional reaction have appeared to give more immediate results than those which were uncomplicated by a chill or rise in temperature

The artificial fever in their study was produced by the Kettering hypertherm and during the period of therapy no other treatment for the colitis was given except a smooth diet. The authors point out that in this work they were using the nonspecific effect of fever, 1 e, its general effect on the body's defense mechanism, rather than its specific killing effect on an organism, as in gonococcal infections They felt, therefore, that relatively short fever sessions at relatively low temperatures would be as effective as long sessions at high temperature levels. The usual method of treatment consisted of two and a half to three hours of fever between 104° F (40° and 40.5° C) and 105 (rectal), three times a week. The number of treatments varied between 7 and 17, the average being 12 per patient

Each of the five patients treated responded very favorably to this type of fever therapy. The clinical improvement preceded the improvement in the proctoscopic appearance. In most cases, after three to four fever treatments in seven to ten days, the number of stools was markedly diminished and bleeding and tenesinus were less. The Reviewer notes, however, that the follow-up period in none of the cases reported was longer than 18 months. The authors emphasize that the use of artificial fever in the treatment of ulcerative colitis is not regarded as a treatment which will produce a permanent cure, but it has been the method which has produced the most rapid clinical improvement in their hands They point out that their short preliminary report is made so that others may attempt this type of therapy

L B Eyerly and H C Breuhaus8 employed rectal instillations of aluminum hydroxide and kaolin in the treatment of ulcerative colitis The technic consisted of first, cleansing the lower colon with a pint of warm water, and in one hour this was followed by a retention enema consisting of a 3- to 5-ounce (90 to 150 Gm) mixture of kaolin and aluminum hydroxide in from 3 to 5 ounces (90 to 150 cc) of warm distilled Their investigations, they concluded, support the belief that this treatment of ulcerative colitis is rational The adsorption of bacteria and their products presumably reduces irritation and decreases the absorption of toxins The astringent action of this preparation, they feel, lessens absorption and the transudate from the inflamed surfaces is diminished

There is no admixture with food and digestive secretions, a neutral reaction in the bowel is preserved, and no toxic effects have been noted

The aluminium hydroxide and kaolin treatment per rectum has also been advocated by W Z Fradkin9 who reported strikingly beneficial results with Fradkın states, however, that this therapeutic procedure is indicated only in the convalescent ulcerative colitis patient, where there is a continued presence of blood in the stools and the number of stools remains above normal He stresses that it is not a cure and should supplement other measures of therapy, and must not be used in the acute stages of the disease The preparation which the author employed consisted of 20 per cent kaolin, ten per cent mineral oil, and 70 per cent of a gel of aluminum hydroxide, equivalent to 21/2 per cent of Al₂(OH)₆

Regarding the technic of administration, Fradkin states that when the patient passed three or more stools in 24 hours, the medication was administered without a preliminary saline enema. Otherwise, a small low saline enema was given about two hours previously, to permit the medication to come in immediate contact with the lesions Six ounces of the mixture was diluted with four ounces of warm water and instilled slowly into the rectum taking 15 to 20 minutes for the procedure If possible this was to The treatment be retained overnight was carried out three times a week and gradually reduced to once a week as improvement was noted. The author reported that blood streaks disappeared usually after the third or fourth week and in a few cases only four or six treatments were necessary When blood streaks did recur, one or two weeks of treatment readily controlled it average number of treatments necessary to control blood-streaked stools was 114 and the average number of weeks required for treatment was 77

Two recent reports in the literature have dealt with the topical application of cod-liver oil in the treatment of ulcerative colitis. In view of the value of cod-liver oil locally in the healing of wounds and chronic skin ulcers, its possible efficiency in chronic ulcerative colitis has been considered R Spiegel10 advocated a 40 per cent emulsion of codliver oil, acacia and water be instilled rectally. For those patients whose lesions had healed, leaving only a slight residual involvement in the lower part of the rectum large suppositories consisting of 68 per cent cod-liver oil were made use In a preliminary report of his results, Spiegel was of the opinion that there is undoubted value in this procedure He is at present experimenting with other fish oils with a greater vitamin concentration

I A Manville¹¹ was equally as enthusiastic over cod-liver oil treatment

He used a spray gun, the tip of which was sufficiently long to protrude beyond the end of the sigmoidoscope, and attached thereto a pressure reduction gauge In this manner the lightest possible spray of oil was introduced, leaving a thin coat applied directly to the mucosa In some instances one-half ounce of cod-liver oil was instilled as an overnight retentive enema. Results in all cases were reported as being distinctly good.

R B. Cattell¹² in a review of the indications for surgery in intractable cases of chronic ulcerative colitis, reports the results at the Lahey Clinic following partial and complete colectomy. In approximately 20 per cent of their cases, some type of surgical procedure has been deemed necessary There are few patients, Cattell states, in whom ileostomy or partial colectomy can be expected to give relief and it is, of course, extremely difficult to estimate the extent of the disease process He expresses the belief that complete colectomy will be necessary in most cases of severe chronic idiopathic ulcerative colitis if the disease is to be entirely eradicated and if this procedure is carried out in stages, directly dependent upon the condition of the patient, it can be done with safety in these poor risk patients

The first stage of colectomy should not be done for months after the ileostomy. The time between the stages of colectomy should not be less than two months and longer periods of time may be of benefit. Since most all cases show marked involvement of the rectum Cattell has not found it feasible to leave a stump of rectum for later possible anastomosis of the ileum to the rectum. Four patients having complete colectomy have been observed for a period of five years following operation. None has had any recurrence of fever,

malaise, prostration or other clinical manifestations of the disease These patients are able to carry on a normal activity after complete recovery. The normal fluid consistence of the ileum changes as the ileum takes over the The author has function of the colon demonstrated dilatation of the lower end of the ileum in these cases and skin irritation around the ileostomy has been unusual after removal of the colon The patients, however, must continue to wear an ileostomy apparatus since they have an average of five stools daily

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CHRONIC GASTRITIS

By WILLIAM A SWALM, M D, and LESTER M MORRISON, M D

Diagnosis — Chronic gastritis gradually is assuming its rightful recognition in the eyes of the American medical profession after years of hesitancy in its acceptance. Its significance and prevalence are now being appreciated and have received an especial impetus since the development of the semiflexible Wolf-Schindler gastroscope in 1932. This instrument at the present time is the most reliable method of diagnosis of gastritis, where surgical removal of gastric tissue is not accomplished, in the vast majority of patients Contributions to the problem of chronic gastritis for 1937 and the latter part of 1936 can be grouped under the main headings (1) Diagnosis and (2) Treatment In the field of diagnosis a review is made under four diagnostic methods (a) By gastroscopy, (b) by histologic study of surgically resected stomachs, (c) by cytologic examination

- of the gastric sediment, (d) by the roentgen ray method
- (a) In the gastroscopic field, Schindler and his collaborators have made a number of observations embracing diagnosis, clinical features from the historical and physical angles and therapy recent textbook, "Gastroscopy," sets forth in a most comprehensive and concise fashion considerations on chronic gastritis However, the book is a compilation of his former 1923 atlas plus all subsequent studies on gastroscopy and does not shed any particularly new light on chronic gastritis, since he reviews in an authoritative manner his own and other past contributions in this field In addition, Schindler, Ortmayer and Renshaw,2 in a study of the complaints in a series of patients with gastroscopically diagnosed gastritis, pointed out the lack of uniformity of the various types of

gastritis They analyzed the histories of 12 patients with chronic superficial gastritis and 23 with chronic hypertrophic gastritis These cases were selected from a group of 349 patients. Extragastric pathology was ruled out in all individuals Among their interesting observations were the notes made that the hypertrophic form of gastris occurs predominantly in the male, and that there is a lack of correlation between the extent and severity of gastritis and the severity of symptoms The pain experienced by these patients varied widely as to duration, intensity, nature, relationship to meals, type of relief, etc These authors again noted the marked discrepancy in frequency of antral gastritis diagnosed through the gastroscope, and by histological study in resected stomachs No explanation is offered and this problem still remains unsettled In a further study of chronic gastritis, Schindler, Ortmayer and Renshaw3 reiterated their belief that there is no characteristic symptomatology and that physical examination, gastric analysis and roentgen studies are of little aid in making the diagnosis Gastroscopy. however, is the only method permitting an accurate and reliable diagnosis Gross and sometimes fatal hemorrhages from gastritis have occurred, perforation, however, does not occur Superficial gastritis can be dangerous and lead to scrious complications. Schindler and his collaborators do not believe that gastric ulcer originates from chronic gastritis Atrophic gastritis, however, may precede gastric carcinoma, as believed by various pathologists. Atrophic gastritis may be responsible for psychoneurosis as well

Morrison, Swalm and Jackson⁴ during a review of 400 gastroscopies performed as a routine on patients with gastrointestinal symptoms, observed a group with a syndrome of hypochromic anemia, achlorhydria and an atrophic

They bring out their belief gastritis that idiopathic hypochromic anemia is the partial expression of a syndrome, and not a disease entity: and that it is as yet an unknown metabolic disturbance in which atrophic gastritis plays an important rôle They consider the possibility of this syndrome as a forerunner of cancer of the stomach, pernicious anemia and combined sclerosis of the cord. The group of 11 patients reported will be studied in the future for the possible development of the above diseases review is also made of the relationship of primary and secondary anemias, achlor- and hypochlorhydrias and atrophic gastritis

Benedict reiterated his findings in a former paper from the Massachusetts General Hospital⁶ showing the frequency of hematemesis and melena as arising from gastritis He again points out the fact that an important and generally unrecognized cause of hemorrhage from the stomach is from gastritis Numerous patients with hematemesis or melena show no peptic ulcer by x-ray diagnosis, autopsy examination of the gastrointestinal tract, gastroscopy, or upon surgical intervention The most frequent types of gastritis responsible for the hemorrhages are the superficial (erosive) and hypertrophic forms

Types—(b) Eusterman,⁷ after reviewing histologic studies on stomachs with gastritis at the Mayo Clinic points out that it is impossible to separate distinctly on a histologic basis, the three types of gastritis These are (1) Acute gastritis (a) exogenous, (b) corrosive, (c) phlegmonous (2) Subacute gastritis usually secondary to obstruction or infection (3) Chronic gastritis (a) primary, (b) secondary

The reason for the difficulty of adhering to the above classification lies in the fact that various degrees and stages of

inflammation are frequently found in the same specimen He points out Simpson's assertion that the use of the terms "acute," "subacute" and "chronic" are open to misinterpretation. These terms are histologically dubious since in no sense do they really indicate the length of clinical history or actual duration of the lesion Many acute, erosive types of gastritis stay this way and persist as acute, erosive forms for years there are cases which quickly change from a condition of normality to the last stage of atrophy. He illustrates Baker's findings at the Mayo Clinic, that 90 per cent of the gastric ulcers were associated with gastritis on histologic studies of the Similarly, 80 per resected stomachs cent of duodenal ulcers were accompanied by antral gastritis. This agrees very well with the findings of Swalm, Jackson and Morrison, who found previously that nine out of ten cases of peptic ulcer are accompanied by gastritis, gastroscopically diagnosed Eusterman believes that evidence is accumulating to support Huist's theory that atrophic gastritis may result in either pernicious anemia or gastrie caremoma. He also agrees with Konjetzny that those forms of nonmalignant, hypertrophic, stenosing pylone lesions originate in and are a sequel of localized chronic, antial gas-Symptomatically, Eusterman divides the gastritis cases as (a) Ulcer or cancer with irregular symptoms, (b) ulcer-like symptoms, (c) cases with pain similar to biliary colic. His comments on therapy are incorporated in the discussion of treatment below

Technic — (c) Monaghan, Bockus, Kornblum and Moffitt⁸ have described a new technic of sectioning sediment of gastric washings in use at the University of Pennsylvania Graduate Hospital Their method is described in detail and requires preparation similar to that used in patho-

logical tissue sections The authors believe that the method may prove a valuable adjunct in the diagnosis of gastritis. and is corroborated by the studies of C Glaessner in Vienna¹⁰ by analagous methods Therapeutic methods of value are discussed and demonstrated in their series of patients with gastritis Secretory changes are discussed and it was observed that clinical improvement usually goes hand in hand with increased secretion in the subacidity patients, but may take place frequently when elevation in secretory curve does not occur. Age was found to be the most significant factor influencing secretory response to treatment Gastric enzymes are always secreted for some time following the disappearance of acid secretion Chronic gastritis with achlorhydria may delay the response to histamine injection more than 30 minutes The authors also believe that hypochromic, microcytic anemia which responds to iron treatment, may have its predisposition in a primary gastritis Cases of extreme gastrectasia and hypochlorhydria are illustrated with the relationship to the stenosing type of gastritis mentioned under (b) in Eusterman's considerations 7

X-ray Findings—(d) The ioentgen 1ay studies of gastritis include the reports of Gutman, Beaugard, and Hardel, Hansen and Simonsen¹¹ and others The inadequacy of the x-ray method in the diagnosis of gastritis, however, has been most ably set forth by Ansprenger and Kırklın 12 Ansprenger gives the result of his observations from the University of Berlin and collaborates with Kirklin who gives the results of his extensive experience at the Mayo Clinic These x-ray studies are based on controls by the gastroscopic method of comparison and by histologic study of surgically resected stomachs They concluded that

- 1. Negative x-ray findings do not rule out gastritis. Stomachs that have severe and widespread damage both by gastroscopic control and under clinical surveillance may prove entirely negative under x-ray diagnosis.
- 2 "Only a small percentage of cases of gastritis can be diagnosed by roentgen examination Slight changes cannot be seen"
- 3 It is impossible to demonstrate mucosal atrophy by roentgen examination.
- 4 In that small group of cases with roentgen demonstration of gastritis, its presence is indicated by the following sign most importantly, localized, ragged, irregular, hypertrophic mucosal folds
- 5 It is rare to be able to demonstrate wart-like granulations, mucosal erosions, and pseudopolypous formations. Tangenital projections on or near the lesser curvature may be seen occasionally and then can be accepted as proof of the presence of an ulcerous gastritis
- 6 The interpretation of indirect signs must be carried out with the greatest caution

Etiology — Neuberger¹³ has made an important and significant contribution in the demonstration that there is a relation between lesions of the stomach and the brain. This is analogous to Harvey Cushing's well-known illustrations of the relationship between brain lesions and peptic ulcer.

Neuberger's work substantiates the theory held by Morrison and Swalm that gastritis can have a dominatingly neurogenic etiology, just as peptic ulcer. They believe that gastritis is one of the predisposers to cancer of the stomach and gastric ulcer in the sense that it prepares the "soil" (gastric mucosa) for the subsequent implantation of cancer and ulcer Einhorn¹⁴ likewise has subscribed to this theory of Matthieu, Faber, Hurst, Konjetzny and others. Barchi¹⁵ in Italy has

demonstrated by the gastroscopic method, aided by gastric analysis, that blows in the epigastric region can produce a gastritis. This original observation has an important medico-legal significance, if it can be corroborated by other investigators

S Morrison and Feldman¹⁶ have reiterated the frequent occurrence of gastritis, corroborating the studies of Swalm,
Jackson and Morrison, who found the
incidence of gastritis in 135 carefully controlled patients, to be 35 per cent. These
latter authors correlated clinical, roentgen, gastroscopic and gastric analysis
findings in their series and demonstrated
the correlation between gastric acidity
and type of gastritis, showing that the
atrophic forms tend towards reduced or
absent free acid and the hypertrophic
forms towards normal or increased
acidity

Swalm, Jackson and Morrison also showed that nine of ten cases with chronic peptic ulcer had a gastritis and that gastritis was the most frequent disorder of the stomach. Many of the so-called gastrointestinal neuroses, nervous dyspepsias and patients with vague gastrointestinal complaints are actually those of chronic gastritis with demonstrable gastric pathology.

Treatment—Among newer contributions on therapy have been the report of Frohlich¹⁸ on the use of larostidin (histidine hydrochloride) and that of Schindler¹⁹ using deep x-ray therapy for intractable ulcerous gastritis. Frohlich in Prague studies his cases gastroscopically before, during and after larostidin therapy. These included one case of the hypertrophic vertucose variety, two cases of erosive gastritis and two cases of the superficial form. Satisfactory results in all cases were reported both subjectively and upon gastroscopic examination of the gastric mucosa and

method enthusiastically the Schindler's case report of mended "cure" by the Coutard method of irradiation of the stomach is being applied in less intensive dosages by the authors in the intractable form of hypertrophic type of gastritis As Schindler points out, the method is not without danger because of the heavy dosage of x-ray used, his case developing a marked gastric atrophy, but becoming asymptomatic, after the most chronic and severe gastric symptoms He also states that frequently surgery in these types of stomachs merely aggravates the symptoms by virtue of the additional postoperative gastritis which always follows urgery of the stomach

Thiers and Chevallier²⁰ have reported a new method in the treatment of allergic gastritis They inject ultrafiltrates made from gastric secretion, following the ingestion of the allergic foods which are known to produce symptoms in these patients. This is done as in the manner or desensitization of hay fever, asthma, etc Weidlinger²¹ of Budapest has done the same thing with reported good results for gastritis on the theory that the stomach is not only an organ for the production of digestive enzymes, but also of hormones which are linked with tissue regeneration. In the 100 cases reported by him, relief from the symptoms were found to be generally rapid, particularly as to pain, sensation of flatulence, debility, malaise, etc. He passes the gastric tube in the fasting patient, removes the tasting residue in a sterile svringe 01 to 0.2 cc of the juice free from bile or mucus is then injected subcutaneously during a course of treatment No local reactions have been encountered After months and even years, renewed injections usually will stop any relapses immediately

Due to limitations in space, the recent therapeutic contributions of Kantor,²²

Cheney,²³ Schindler,¹ Hartfall,²⁴ Simpson,²⁵ Brown,²⁶ Eusterman,²⁷ Brunner-Ornstein,²⁸ Moutier²⁹ and Chevallier,³⁰ Peosner and Gordon,³¹ Darling,³² Swalm and Morrison³³ and others are abstracted and summarized as follows:

1 Removal of all possible etiologic factors as—

- (a) Foci of infection in mouth (oral sepsis), teeth, gum, tonsils, nasal accessory sinuses, etc
- (b) Interdiction of smoking and alcoholic beverages
- (c) Faulty habits of hygiene, inadequate mastication, irregularity of mealtime, food bolting, chronic dietary indiscretions, possibly food allergy, etc
- (d) Reflex and contiguous pathology as duodenal disease (ulcer, parasites, etc.), gall-tract disease (infection, inflammation, etc., with continued biliary regurgitation)
- (e) Correction of autonomic nerve imbalance and psychological abnormalities
- 2 Bland diet, nutritious and emphasizing small frequent feedings:
- (a) The atrophic, achlorhydric forms may add seasoning to food, to increase appetite, gastric secretions and weight
- (b) The hypertrophic forms involving the ulcerative and erosive varieties should be managed as peptic ulcer cases with bed rest
- 3 Medication varies with degree of acidity, e g, dilute hydrochloric acid (USP) is given in the atrophic and achlorhydric forms, whereas antacid adsorbents or alkali powders with minimal absorbability are indicated in hyperacidity. Included are vitamins (especially B, B₂), and C (Cevitamic acid) in all erosive and hemorrhagic types, colloidal kaolin with aluminum hydroxide, antispasmodics (tr. belladonna, atropine, etc.), iron (ferrous sulfate preferably), sedatives (pheno-

barbital, bromides), digestants as pepsın. etc

- 4. Gastric lavages, twice and three times weekly in achlorhydric marked hypochlorhydric types. Excessive mucus, regurgitated bile, retained secretions, etc., are thus removed, avoiding irritant effects and a return to function of the acid-secreting glands may be thus accomplished Hydrogen peroxide—one ounce to the pint of warm water, is best The weak silver solutions may be used, but the danger of argyrıa must be borne in mind.
- 5 Spa waters, as Vichy, Kalak, Carlsbad, Saratoga Springs, etc., for their lavaging effect and mineral content
- 6 Physical therapy—local heat by baking, moist applications, diathermy, all for pain (high voltage x-ray for intractable hypertrophic forms still in experimental stages)
- 7 Surgery to be used only in very severe and intractable cases with severe ulcerative and chronic hemorrhagic features Postoperative inflammatory reactions locally, however, must be expected
- 8 Prophylaxis—the possible development into peptic ulcer, gastric carcinoma, or pernicious anemia in some forms, indicates that the principle of periodic health examinations should specifically be applied in these cases Hence gastroscopic examinations and x-ray studies should be repeated at stated intervals. depending on the financial circumstances Preventive medicine of the patients here is all-important

In conclusion, the recent findings of Kark34 at Guy's Hospital and of Comfort and Butsch³⁵ at the Mayo Clinic are of great significance, regarding the theory that gastritis is the forerunner of primary anemia and of cancer of the stomach In the main, all proof of this belief has been offered by the European

investigators Kark's report embraces aplastic anemia with secondary gastric carcinoma following atrophic gastritis Comfort and Butsch report two proven cases in which histological study of resected biopsy specimens at the first operation on the stomach showed a marked gastritis. In approximately one year reoperation was performed for persisting gastric symptoms and in each case gastric carcinoma was present proven histologically

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DISTURBANCES OF LIVER FUNCTION

By HINRY J TIMEN, M D

Serum Bilirubin — Although the technic developed by Thannhauser and Anderson did much to increase the accuracy of the van den Bergh test, this method of serum bilirubin determination is still somewhat imperfect. The chief sources of error of the van den Bergh test arise from the loss of color by adsorption on the precipitated protein, alteration in color of the diazo-bilirubin compound because of changes in the pH of the solution and the use of artificial standards. In order to avoid these inaccuracies various improvements in tech-

nic have been suggested 1, 2, 3, 4 These have to do chiefly with the use of photometric methods for bilirubin estimation. This renders unnecessary the use of an artificial standard and also removes the errors dependent upon differences in color perception by individual observers. Malloy and Evelyn¹ report a new method of diluting the serum that tends to decrease the bilirubin loss by protein adsorption.

Jendrassik and Cleghorn³ have described a photometric method for bilirubin determination in which sodium

caffeine benzoate is used as a catalyst It is claimed that this method is extremely accurate and permits the separate determination of the indirect and direct reacting types of bilirubin A great deal of evidence has accumulated in the past that tends to indicate that these two pigments have definite physical differences and some substantiation of this opinion is offered by the spectrophotometric studies of Davis and Sheard 5 A method for separately determining the amounts of direct and indirect reacting bilirubin in the serum would be of extreme value in the differential diagnosis of jaundice Attempts have been made to utilize various properties of the pigments in order to make such a determination It is probable that methods dependent upon dialysis are not satisfactory 6 In a previous review of this subject⁷ the work of Varela-Fuentes was referred He has indicated that the solubility of indirect-reacting bilirubin in chloroform offers a means for its separate estimation Utilization of this procedure in small groups of cases has shown that indirect-reacting pigment may be present in the serum in appreciable amounts even though the gross qualitative reaction is of the 'direct type "8, 9 If further use demonstrates the accuracy of the method employed it would seem to offer a new approach to the solution of some of the problems of icterus and, possibly, aid in the differentiation of obstructive and hepatocellular jaundice

Urobilinogen Determination—Watson¹⁰ has developed an improved method for the quantitative determination of urobilinogen in urine and feces. Although not a method that has wide clinical applicability its use in normal individuals and in a group with hepatic disease led Watson to conclusions that seem more reliable than those obtainable with the ordinary test which utilizes the

color reaction to Ehrlich's aldehyde reagent. Watson found that the normal urobilinogen excretion in the urine varies from 0 to 4 mg daily and is usually between 05 to 2 mg. He also noted that jaundice due to stone was not marked by much increase in urobilinogenuria unless a complication such as acute cholecystitis or cholangitis or biliary cirrhosis developed Watson found that icterus due to stone was rarely associated with complete obstruction to bile flow although this was the rule in malignant obstruction and that in the latter condition urobilinogen practically disappeared from both feces and urine In liver cell disease, both acute and chronic, increased urobilinogenuria was usually observed Watson also found the urine content of urobilinogen to be increased in hemolytic He did not consider this to be a result of increased blood destruction but due to associated disturbance of liver function Watson's studies are an important contribution to the investigation of this phase of liver function. The value of routine urine urobilinogen determinations as a liver function test is, however, probably not as great as was formerly believed Examination of single urine specimens frequently fails to give information of assistance in diagnosing liver disease Persistent absence of urobilingen from the urine of a jaundiced patient is of significance, on the other hand, in that it suggests the presence of a malignant form of biliary obstruction

Tests Based Upon the Utilization of Sugars—Jacobi¹¹ has suggested the use of a modification of the glucose tolerance test in the differential diagnosis of Jaundice. He recommends giving 100 cm of glucose, taking blood specimens for sugar determinations before the glucose and at 45 minutes and two hours after its ingestion. Jacobi feels that patients with toxic hepatitis are capable

of utilizing large amounts of glucose and that a characteristic feature of these cases is a return of blood sugar level to normal within two hours of the ingestion of glucose In extremely severe instances of hepatitis the blood sugar level even at 45 minutes may be only slightly above the original determination. In obstructive jaundice, on the contrary, the blood sugar is still definitely above the fasting level at the end of two hours Jacobi believes that the finding in a naundiced patient of a blood sugar curve of the type he considers diagnostic of hepatitis is a definite contraindication to surgical intervention

The galactose test continues to be regarded as an extremely reliable aid in differentiating jaundice due to acute liver cell disturbance from that due to obstruction White12 reported the galactose test to be positive in a majority of patients with acute infectious hepatitis, particularly if performed early in the course of the icterus. The test was rarely positive, however, in patients with biliary obstruction. White's conclusion that a positive galactose test in a jaundiced patient indicates the presence of hepatocellular damage but that a negative test doesn't necessarily exclude liver injury, is similar to the opinion most widely Because of the possibility that glycosuria after galactose administration may occasionally be sufficient to cause an apparently positive response to the test, it has been suggested that differential fermentation of the urine with veast be done routinely in all instances in which a positive result (excretion of 3 + grams) is reported 13 This procedure is of particular value in diabetes, nyperthyroidism and patients with renal gly cosuria and should be employed whenever the galactose test is done on patients whose urine may contain glucose

Galactose has largely replaced levulose in the testing of liver function. Two reasons for this have been the digestive disturbances that frequently follow levulose administration and the fact that difficulty has been experienced in determining the normal blood sugar changes after ingestion of this sugar Steinitz,14 however, has reported the levulose tolerance test to be a satisfactory one Using a 60 Gm dose of the sugar he considered as normal a rise of 6 to 10 mg per cent in the venous blood sugar In acute liver disease the blood sugar rise was rapid and marked and returned to normal in little more than two hours. In chronic conditions the blood sugar increase was slow and not as marked, but the return to the fasting level was quite protracted Stewart¹⁵ and his coworkers report a method for the separate determination of levulose in the blood They felt that this was necessary because levulose feeding is usually followed by changes in the blood glucose level so that measuring the total blood sugar leads to inaccuracies With a 50 Gm dose of the test sugar the maximum blood levulose level in the normal individuals was found to be 20 mg per cent This normal maximum was found to be exceeded in the small group of patients with liver disease studied by them

Hippuric Acid—The earlier work on this test has already been reviewed ⁷ In their investigations of the value of the hippuric acid test Yardumian and Rosenthal¹⁶ found it to be of value in the differentiation of intrahepatic and extrahepatic jaundice. In the former type of icterus the excretion of hippuric acid was found to be quite low but in acute obstruction its urinary excretion was normal. They also concluded that the test might be of assistance in measuring the development of secondary liver injury in chronic biliary ob-

struction since if this occurred hippuric acid excretion decreased. The authors felt that the presence of congestive heart failure or of severe renal disease interferes with the utilization of this method of liver function investigation since both conditions caused decrease in hippuric acid elimination Bartles and Perkins¹⁷ used the hippuric acid test to study the incidence of liver dysfunction in patients with hyperthyroidism In agreement with the reports of the pathological investigations of others18 they found that liver injury was present fairly frequently in Grave's disease It was found that the hippuric acid test was of real assistance in evaluating the results of preoperative preparation of these patients since as a decrease in metabolic activity and rise in blood cholesterol occurred, hippuric acid excretion increased to proportionate degree

Serum Protein Levels and the Takata Reaction Recent studies have served to emphasize the frequency with which changes in the levels of the serum proteins occur in hepatic disease and the diagnostic significance of such changes Thus, Tumen and Bockus¹⁹ found that hypoalbummenna was found in every case of chronic advanced liver disease and in many of the patients with obstructive jaundice or acute hepatocellular damage studied by them This finding was encountered more frequently in hepatic disease than elevation of the serum globulin or inversion of the albumin-globulin ratio The investigations of Foley and his associates20 gave substantially the same results. The albumin decrease is found so consistently in patients with severe hepatic disease that one seems justified in assigning diagnostic significance to this change in the blood Kendall²¹ has reported changes in both the quantities and proportions of the globulin fractions in the blood

serum of patients with cirrhosis. Much of the clinical evidence, particularly the fact that a high protein diet fails to elevate the serum albumin level, points to the conclusion that inability of the damaged liver to manufacture albumin or its precursors is at least largely responsible for the hypoalbuminemia found so frequently in hepatic disease This opinion finds some confirmation in the report of Luck and Martin²² that low reserves of albumin are found in the damaged livers. The significance of decreased serum albumin in the production of ascites in cirrhosis was emphasized in the earlier studies of Myers and Keefer 23 More recent investigations^{24, 25} have shown that in cirrhosis there is a disproportionate decrease in colloidal osmotic pressure of the serum It would seem that this factor is at least equal in importance to portal hypertension in causing the development of ascites in advanced hepatic disease

Bowman and Bray²⁶ have recently reported their experiences with the In their hands the Takata reaction test did not have much diagnostic value since it was not strongly positive in three cases of cirrhosis confirmed by autopsy but was positive in numerous noncirrhotic patients of the most variable types who had lowering of the total protein or of the albumin-globulin ratio Since the diagnoses in most of these cases were purely clinical it is impossible to be sure that many of the patients reported by these authors did not have hepatic damage Their conclusion that the test has little diagnostic value does not agree with other opinions recently expressed 27, 28 Thus Gertler and Lachenicht found a positive Takata reaction in cirrhosis, icterus simplex and carcinoma of the liver and decided that such a reaction always indicates the presence of severe liver disease. At present it would seem that the only diseases other than those of the liver in which a positive Takata reaction occurs with any frequency are multiple myeloma and lymphopathia venerea. The test does not seem to be of very great assistance in diagnosing liver disease, however, since it is rarely positive unless there is also other evidence of hepatic dysfunction

The investigations of Gros²⁹ have done much to clarify the character of the changes in the serum proteins which are responsible for a positive Takata reaction Such a reaction is certainly not dependent solely upon a relative increase in total globulin, decrease in albumin and reversal of albumin-globulin ratio has shown that the most usually found serum protein change in cases with a positive Takata is an increase in the This is normally cuglobulin fraction 0.08 to 0.32 (m) per cent, comprising 10 to 15 per cent of the total globulin In those cases with a positive Takata reaction the euglobulin was found by thos to range from 0.30 to 5.55 Gm per cent and was more than 10 Gm per cent Since the increase in in most cases cuglobulm was found in all cases with a positive Takata independent of the nature or the underlying disease and was absent when the Takata test was negative even though the total globulin might be increased. Gros concluded that the increase in englobulin was the factor responsible for a positive response to this test

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PEPTIC ULCER

By Thomas A Johnson, AB, MD

Etiology—The obscure etiology of peptic ulcer and the resulting uncertainty and lack of specificity of treatment in a measure account for much speculation and experiment on the part of the active investigators. The current literature is replete with reports of those efforts. Nevertheless, one feels that there is little reason to depart from the usually accepted methods of management of peptic ulcer.

Davies and A Wilson¹ studied the etiology of 205 cases of peptic ulcer from the viewpoint of possible psychic trauma in the form of anxiety due to financial, family or employment problems, and found that in 84 per cent of their cases the onset of ulcer symptoms followed such episodes Of a group of hermas similarly studied, only 22 per cent gave such a history. The authors concluded that peptic ulcer might represent the result of the effect of the mind in producing structural change, and that successful ulcer therapy depended, in part at least, on attention being given to the psyche

John² reported a case of chronic duodenal ulcer in a child aged six years. The patient died following an appendectomy and at autopsy a chronic ulcer was found on the posterior duodenal wall, nine millimeters beyond the pylorus. The author quoted numerous authorities who commented on the extreme rarity of chronic ulcer in the first decade of life, and he believes his case to be one of the earliest ever reported

Pathogenesis - Numerous investigators have focused their attention on the rôle of vitamin C as a contributory factor in the pathogenesis of peptic ulcer, particularly with respect to hemorrhage H E Archer and G Graham,3 reviewing their autopsy material on patients who died as a result of operations for peptic ulcer, noted the marked similarity of the unhealed suture lines to those observed in scurvy They reviewed experimental animal work wherein proof was offered to support the belief that lack of vitamin C promoted incomplete or unsatisfactory wound healing However, Archer and Graham from their data were unable to conclude that a subscurvy state was responsible for the development of peptic ulcer, or that the ulcers healed more quickly and were more likely to remain healed following the administration of vitamin C

G Bourne⁴ concurred in that view-point, but felt that it was more likely that the deficiency in antiscorbutic vitamin in the therapeutic diet may be a factor influencing the transition from the acute to the chronic condition, predisposing to delay in healing, relapses and possible hematemesis. As yet we have no

definite clinical or experimental proof of that relationship

Platt⁵ noted the not infrequent occurrence of a prescorbutic state and even frank scurvy resulting from therapeutic ulcer diets in which the administration of vitamin C was overlooked A B Rivers and L A Carlson⁶ state that vitamin C is important for its effect on cellular respiration, cellular integrity, and capillary structure. Any ulcer regimen is inadequate if it lacks an adequate amount of vitamin C

B Portnoy and J F Wilkinson⁷ investigated the vitamin C tolerance of 107 subjects, of whom 51 were controls, 25 had proven peptic ulcer and 31 were admitted to the hospital with hematemesis. They found that the ulcer and hematemesis patients suffered from severe vitamin C deficiency but that the severest degrees of vitamin C deficiency appeared in the patients with hematemesis.

S Lazarus' came to a similar conclusion after studying his group of hematemesis cases and in addition noted that not introquently the soft diet given those patients while in the hospital was madequate to supply the normal body requirements of vitamin C

It appears that, while proof is lacking that a deficiency of vitamin C is the most important factor in the etiology of ulcer hematemesis, adequate evidence has been presented that not infrequently the usually prescribed ulcer diet induces a prescribid ulcer diet induces a prescribid ulcer and Graham (local) advise giving ulcer patients initial doses of 1000 mg of vitamin C daily tor three successive days, followed by a daily dose of 36 to 40 mg of vitamin C may be given in the form of two ounces of *orange juice* daily

A hormonal mechanism associated with peptic ulcer is suggested by the recently reported work of D J Sand-

weiss, H C Saltzstein, and A Farbman 9 Having noted that peptic ulcer and its complications were infrequent during the course of pregnancy, they treated each of two groups of Mann-Williamson dogs with estrogenic and gonadotropic hormones, both of which are excreted in increased amounts during pregnancy Twelve untreated controls died of typical jejunal ulcers Fifteen Mann-Williamson dogs treated with theelin died with typical jejunal ulcers, however, those dogs died sooner than the control dogs, indicating that theelin (estrogenic) accelerated the pathology Fifteen dogs were treated with antuitrin-S (gonadotropic anterior pituitarylike hormone), of which 53 per cent showed evidence of no ulcer at autopsy (performed after the dogs died of inanition), four dogs died of ulcer but there was some evidence of attempted healing of the ulcers

The above work of Sandweiss et al, if confirmed, is of tremendous therapeutic importance. One hopes that there will not follow in its wake a wave of uncritical subcutaneous peptic ulcer therapy before suitable clinical investigations have been carried out.

Diagnosis—A R Peskin¹⁰ reports a group of cases illustrating the frequency with which some of the symptoms of mild hypoglycemia mimic those of peptic ulcer There are substantial differences in the behavior of the former group of patients in comparison with the latter, namely the partiality for highly spiced foods, lack of seasonal periodicity, the daily occurrence of pain, frequent occurrence of multiple attacks of nocturnal pain with food relief, lack of relief from alkalis, and the tendency to diminution in acidity even to the point of achlorhydria In a carefully studied case there is little excuse for confusion between the two entities if both are kept in mind by the attending physician.

A Holman¹¹ reviewed his group of 152 patients in which it was necessary to differentiate between benign and malignant gastric lesions Using the continuous extraction technic of gastric analvsis, developed by Bloomfield and Pollard in 1929, he showed that none of the 90 benign ulcer cases had a low acid and with the exception of five cases the remainder of the proven 62 cases of gastric carcinoma showed a low or absent hydrochloric acid After reviewing the usual clinical criteria of differentiation between benign and malignant gastric lesions, the author concludes that gastric analysis by the above technic. although not infallible, is as accurate as any method yet developed

J R Kahn¹² reviewed the charts of 840 patients with pernicious anemia, admitted to nine hospitals over a period of 15 years. Six hundred and sixteen cases had achlorhydria, while 224 cases did not have a gastric analysis. In none of the 840 patients was a diagnosis of chronic peptic ulcer made and in only two cases was there any history at any time of an ulcerative lesion of the stomach. The author believes that the study is significant of the relation of hydrochloric acid to peptic ulcer.

S E Johnson¹³ studied 42 cases of perforated gastric or duodenal ulcer and found air under the diaphragm in 35 instances or 83 per cent of his cases

The end results of subtotal gastrectomy are reported by E A Gorvett and E S Talbot¹⁴ in connection with their 26 cases (16 for duodenal ulcer and ten for gastric ulcer) with the following interesting conclusions

1 Sixty-five per cent had postoperative achlorhydria

- 2. The achlorhydria was more common in the gastric than in the duodenal cases
- 3. A high preoperative acid curve did not necessarily mean a high postoperative acid curve
- 4 Reflux of bile is a definite factor in the interpretation or production of an achlorhydria.
- 5 Only one relative secondary anemia was observed.
- 6 The postoperative emptying time of the stomach was usually decreased
- 7. No postoperative dilation or hypertrophy was observed
- 8 Fifty-eight per cent of the patients gave a history of some form of intestinal unrest
- 9 Two of the 26 cases had recurrent marginal or jejunal ulcer
- 10 Of the 26 cases, nine were followed over a period of five years, 11 from one to five years, and six cases less than one year

Treatment—The management of the various complications of peptic ulcer has undergone very little recent change. In an excellent article on hematemesis and melena, L. J. Witts¹⁵ thus summarizes

- 1 Mass hospital statistics are of little value in determining the relative merits of operative and nonoperative treatment of gastroduodenal hemorrhage
- 2 The best individual medical results (Meulengracht, 1936) are superior to the best individual surgical results (Fursterer, 1936)
- 3 It is rarely possible to differentiate between acute and chronic ulcer in the first 24 hours following hemorrhage
- 4 Do not center treatment too much on the bleeding point but rather on the patient himself. The treatment of the hemorrhagic shock is of immediate importance.

5 Continued efforts should be directed toward the prevention and treatment of recurrent bleeding

Witts further elaborates on the chemical aspects of the adequate treatment of hemorrhage

F H Kruse¹⁶ states that the true incidence of hemorrhage in all ulcers is near ten per cent, although most authorities place it nearer 25 per cent Kruse states further that he favors conservative procedures in the management of hemorrhage, "although the results reported by Meulengracht of Copenhagen of the treatment of 251 patients with hemorrhage by use of rest in bed and liberal diets from the first day, with only one per cent mortality as against the usual five or ten per cent, should lead to a critical test of the wisdom of starvation, with its concomitants of exhaustion and aneima as its least serious asticets."

The indications for surgery in peptic ulcer have not undergone any recent radical change and, as well stated by F I alicy ¹⁷ are "a continuation of symptoms in spite of medical management, the presence of a definite pyloric obstruction perforation, hemorrhage in spite of good medical management, and in gastric ulcer the suspicion of the association of malignancy with the ulcer"

The use of *laevo-histidine-monohy-drochloride* (*larostidin*) in the treatment of peptic ulcer dates from the experimental work of Weiss and Aron¹⁸ in 1933. It is now possible to evaluate that type of therapy in terms of something more than the immediately successful amelioration of symptoms which initially seemed quite impressive to many workers. Important critical contributions by E. W. Willhelmy, ¹⁹ J. T. Eads, ²⁰ D. J. Sandweiss, ^{21, 22} L. Goodman and P. A. Bearg-²³ and K. A.

 $Martin^{24}$ summarize the current opinion of the ultimate value of that preparation

- E. W Willhelmy (loc cit) using parenteral histidine was able to produce remissions in a fairly high percentage of uncomplicated ulcer patients, but the results were no better than those observed with ordinary ulcer management Moreover, he produced a remission in only one case out of four in which a dietary and alkalı regimen previously had failed to give relief On the basis of his observations. Willhelmy declared that the routine use of histidine was not justified T Eads (loc cit) followed cases for varying periods of 6 to 18 months and found that the early favorable results of histidine treatment failed to continue in 35 per cent to 65 per cent of cases He concluded that the end results of histidine treatment were less lasting than those following the regular dietary and alkaline routine
- I) J Sandweiss (*loc cit*) in one of the most comprehensive studies on the clinical use of histidine, in part, drew the following conclusions
- 1 Ninety per cent of patients with attacks of peptic ulcer become symptomfree on careful dietetic-alkali management
- 2 Of those given parenteral injections after failure to respond to the diet-alkali regimen 60 per cent became symptom-free after injections of either stock respiratory vaccine, larostidin (histidine), or synodal. In 22 patients, injections of distilled water were used with comparable results
- 3 There is an undoubted psychic effect to be expected with parenteral injections, i e, the effect of something new and unusual
- 4 Most ulcer patients have recurrences under any form of treatment but the parenteral group had earlier recurrences, due probably to the lack of

proper dietary restrictions The failure of the recurrent ulcer patient to remain on a restricted diet even in his symptomfree period is emphasized

L Goodman and P A Beary (loc cut), following up the original work of A G Weiss and E Aron,18 in dogs with accessory stomachs and gastrostomized preparations found that the administration of parenteral histidine did not decrease the volume or acidity of the gastric secretory response either to food or histamin stimulations

Kirby A Martin (loc cit) reviewed his experience in the treatment of 41 cases of peptic ulcer with parenteral histidine and came to conclusions not greatly at variance with those reported by Sandweiss (loc cit)

Undoubtedly the early enthusiastic acceptance of the claims of the advocates of the use of histidine engendered in the minds of some physicians and patients a false sense of security which, coupled with a lack of proper perspective in arranging an all-inclusive ulcer regimen, undoubtedly led to an earlier appreciation of the fallacy of a 24-injection cure of this stubborn chronic disease than otherwise would have occurred

The sine qua non position of acid neutralizers in successful peptic ulcer therapy encourages efforts to develop more satisfactory chemical agents. The ultimate estimation of the value of colloidal aluminum hydroxide therapy has yet to be made. There are those who cannot avoid the thought that the continued use of an astringent substance, such as colloidal aluminum hydroxide over a period of years might lead to atrophic changes in the gastric mucosa It will be interesting ten years hence to further investigate that possibility C R Jones²⁵ notes the rapidity with which this type of therapy lessens the pain of ulcer J M Beazell, C R Schmidt, and A. C Ivy²⁶ concluded from a study on dogs that colloidal aluminum hydroxide did not absorb digestive enzymes. Numerous investigators attest to the value of a 24-hour aluminum hydroxide drip in an attempt to control the excessive acidity due to hypersecretion.

The work of N Mutch^{27, 28, 29} has stimulated investigation of the absorptive potentialities of magnesium trisilicate either as such or in combination with other antacids. M B Levin³⁰ emphasizes the necessity of an antacid powder that combines the effect of immediate acid neutralization with the slower effect of later adsorption Given a rapidly emptying stomach, it is not clear to the Reviewer exactly what benefit might be expected to accrue from the use of a substance which requires four to five hours or longer to exert its full chemical effect Perhaps that will be cleared up in future contributions

R T Monroe and E S Emery³¹ reviewed 1428 cases of peptic ulcer studied at the Peter Bent Brigham Hospital during the period 1913 to 1932, and found that while 161 (113 per cent) died, only 87 (61 per cent) deaths were caused directly by the ulcer Of the ulcer deaths 33 per cent were the result of perforation, 25 per cent to hemorrhage, only five per cent to obstruction The authors also concluded on the basis of that study that the duration of life in patients dying as a result of peptic ulcer compares favorably with that given for all individuals in insurance tables

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By Carroll Spaulding Wright, BS, MD

The past year has been a significant one for venereal diseases. For many years attempts to control venereal discase hy public health authorities have been handicapped by public apathy and indifference and reluctance to discuss the problem or do anything about it" It the conference on venereal disease control work called in Washington December 28 to 30, 1936, Dr Thomas Parran, Surgeon General of the United States l'ublic Health Service in his address of welcome after the above quoted remark, stated further that "recently the situation has changed very rapidly The idea is catching the American people that syphilis is a disease which can be controlled if proper efforts are applied to that end We have seen a remarkable increase in public interest and public concern We are seeing definite signs of public demand for action by the health agencies, by the medical profession, and others concerned with this problem. This conference has been called to devote itself primarily to a consideration of the principles which should underlie a national plan for the control of the venereal diseases

"Public interest seems to be running ahead of the provision of community facilities for the diagnosis and treatment of these diseases We are told by leaders of the medical profession that many physicians are not prepared to give modern diagnosis and treatment. We have learned from check tests that many State and private laboratories are inaccurate in their examinations. The examinations for syphilis are so insensitive in some laboratories that cases of syphilis are In others they are so hypersensitive that certain persons who are not suffering from the disease are labeled as syphilitic In other words, the laboratory facilities of the country need to be

improved Relatively few health departments are prepared adequately to deal with the problem. We have not developed more than a handful of captains and lieutenants and very few corporals or even privates in the ranks who are needed to assist in the control of these diseases. We find many hospitals still unwilling to admit cases frankly diagnosed as syphilis or gonorrhea although inevitably these hospitals continue to treat end-results.

"We find many prenatal clinics still not applying a routine Wassermann test on their admissions and the same thing is true in private practice"

Those are some of the problems discussed at the conference and in this review of the past year important phases will be referred to frequently

There can be no question that public opinion in regard to syphilis has changed considerably as a result of Dr Parran's fight to control venereal diseases past year has seen co-operation by press and radio P de Kruif and T Parran.1 in discussing the subject of "public cooperation in the control of syphilis," state that "to get the deep enthusiastic co-working of the whole people it is necessary to tell the people all of the truth Scientific and medical teachers of the people have got to be candid, absolutely, about such defects in their technical weapons as exist More important still, while proud of the present wondertul growth in medical co-operation, they must admit such shortcomings as unquestionably prevail in the rank and file and even among the nabobs of the professions of public health and healing So that their good intentions to instruct may not boomerang upon the public's would-be instructors, the present incompetence of many of the medical profession to detect syphilis must be admitted. And medical venality that so often cuts treatment short of the point needed to make the plague noninfectious has got to be acknowledged

"With the ground thus cleared, with all cards face up on the table, with promise of a fight as stern against professional incompetence as against the spirochete itself, then, and only then, can mass co-operation be expected, and then real battle for eradication will be ready to be planned"

Wile (Ibid) considers the problem of "Co-operation of the Private Physician" and states that "the whole-hearted cooperation of the private physician in the program of national control of a communicable disease is not only an imperative necessity, but carries with it an obligation of public and private responsibility In assuming the care of a case of communicable disease, the physician assumes a dual responsibility. He is obligated to the patient in the first place, to carry through with him until such time as he ceases to be a public health problem His second responsibility, a more public one, is, by strict adherence to existing regulations, to carry out such measures as are prescribed by health authorities so that during the patient's infective period he is of little or no risk to those with whom he comes in contact The problem of venereal disease control, from the standpoint of protection of those in contact with the affected individual, is a more difficult problem in many ways than that of such communicable diseases as demand isolation and quarantine In the care and control of venereal diseases during the infective period, the responsibility of the physician rests not only with such remedial measures as are at hand to render the patient noninfective in the shortest possible time, but, because of the peculiar and intimate methods of possible transmission, to impress upon the patient a

sense of personal responsibility which is the best safeguard against his exposing others to his infection.

"From the standpoint of vital statistics, and for the immediate purposes of the study of venereal disease incidence, it is of paramount importance to recognize that earnest and sincere co-operation on the part of the practicing physician is required to fulfill the obligation of reporting, which is of first importance in the control of any communicable disease There is no doubt that considerable reluctance, based upon the traditional relationship between physician and patient, still exists which may retard the immediate success of venereal dis-Nevertheless. in the ease reporting light of public interest and of an awakened public consciousness, this tradition is being modified where public interest so requires Reporting by name already exists in some States, and there can now be no legitimate objection to reporting, at least by initial or number and address, under all circumstances with the condition that such information remains of a confidential nature so far as public health officials are concerned, and can in no way be used to endanger the reputation or character of those concerned

The obligation of the private physician in his co-operation in venereal discase control is, therefore, a clean-cut one. This obligation, however, is by no means one-sided. On the part of the public health officials, an obligation also exists. This should be to place at the hands of physicians at all times, such resources, information, and assistance as may be available through public funds. At all times the effort should be made to conserve, as far as possible, the time-honored relationship of patient and physician.

"By united effort, therefore, and by cordial co-operation between the public health agencies on the one hand and the private physician on the other, the objective of control seems well within reach, notwithstanding the ethical and personal considerations which thus far have handicapped a united public approach to the problem"

Research Needs in the Control of Syphilis

We know the cause of syphilis, we know how it is spread, we have excellent diagnostic methods for its recognition, and we have effective therapeutic agents for eliminating it from the human body Why, asks A M Chesney,2 has not syphilis become as extinct as the dodo? He goes on to cite the fields of investigation in syphilis that deserve cultivation to close the gaps in our present-day knowledge of syphilis and to improve the application of existing knowledge Unquestionably the one great obstacle to the successful study of the life processes of the spirochaeta pallida has been the difficulty of growing that organism Some investigators doubt that it has ever been cultivated. It is not possible to cultivate virulent forms of treponema pallidum in the sense that one is able to cultivate virulent pneumococci If the problem can be successfully solved, there should be an immediate extension of our knowledge concerning the etiologic agent We do not know why of syphilis spirochetes prefer to localize in certain organs or tissues and habitually leave others severely alone Nor do we know why in one individual the spirochete will tend to localize in one part of the body whereas in other individuals it will tend to localize in other parts

One would particularly like to know the underlying facts governing the pathogenesis of syphilitic lesions of the central

nervous system Why is it that a considerable proportion of syphilitic patients escape involvement of the nervous system? With the organisms coursing around in the circulating blood it seems surprising that the nervous system is not involved in every case. The reason why it is not so involved is quite obscure at the moment

There is one line of investigation in connection with the localization of syphilitic lesions which offers the possibility of an experimental approach and deserves further study. That line makes use of the well-known observation that there is a close relationship between the occurrence of trauma and the development of syphilitic lesions. Why should a nonspecific inflammatory process following injury be favorable to the spirochetes of syphilis?

Outte apart from the narrower technical question of what is the best method for the serologic diagnosis of syphilis, a question which is charged with dynamite in practical serologic circles, there is the larger problem of the nature of the serologic reaction in syphilis and its relation to immunity. I think it fair to say that while at the present time we have some attractive explanations for the mechanism of the Wassermann reaction and the various flocculation tests, we are still in the dark as to the essential nature of these reactions. Do they represent true antigen-antibody reactions? And what is the nature of the hypothetical substance that we go glibly speak of as "reagin"? Is it an antibody to the spirochete of syphilis in the sense that agglutinins for typhoid bacilli are antibodies? We know that it is engendered as a result of inflammatory reaction to the spirochete of syphilis, we can make rough quantitative measurements of it, and we associate it with the globulin fraction of the serum protein Some

think that it is an antibody to lipoids either those of the body itself or those of the spirochetes, but the matter is still uncertain. Moreover, we need to know the relation of this hypothetical substance to immunity to syphilis. Is it, on the one hand, a measure of the host's resistance to his infection or, on the other, a measure of the extent of the harm which has been done to his tissues. We cannot say at the moment, but surely we have here a fertile field for investigation

We cannot say much about the mechanism of the defensive reaction against the spirochete A priori one might expect to find evidence of protective antibodies in the blood of patients or animals that had acquired a specific resistance against syphilis, but thus far the results in this respect have been extremely disappointing. It looks as though the tissues were the site of the defensive process, but the extent to which the individual parts of the body participate in the reaction has still to be worked out It is also important to find out, if possible, why acquired resistance to syphilitic infection breaks down in some individuals and relapses make their appearance, and how it happens that often in these patients the relapsing lesion takes on the characteristics of an allergic phenomenon with excessive tissue reaction to a minimal number of spirochetes The study of these and related questions is imperative if we are to obtain an adequate understanding of immunity in syphilis

The question may be raised whether there may not be more cases of syphilis contracted from persons without open lesions than is generally supposed at the present time. It is at least possible that there may be an appreciable number of carriers of treponemes, especially women, who do not have visible mucous mem-

brane lesions but who, nevertheless, discharge virulent treponemes either continuously or intermittently. The problem of the latent syphilitic as a carrier received some attention in this country about fifteen years ago, but it has never been sufficiently studied, in my opinion, and it is to be hoped that some one will undertake it in the near future. It is well to remind ourselves that practically no attempt has been made to discover a method of prophylaxis against syphilis which would be effective in women. Is the problem insoluble?

When we come to consider the status of our knowledge concerning the treatment of syphilis, we must, if we are candid, admit that there is still much that is obscure

We are still in the dark as to the essential mechanism of the antisyphilitic action of many of the agents upon which we must lean so heavily. There is need for sustained and intensive investigation in this field, for a real understanding of how any one of these agents excits its beneficial action would undoubtedly be of greatest assistance in the search for more effective antisyphilitic drugs than those we now have. The necessity of carrying out such a search will hardly be demed by those who have to treat patients with syphilis. One of the greatest obstacles to the successful control of that disease is the high cost of our present method of treatment and the time that is required for its completion is small wonder that patients who feel well balk at the idea of having to take week after week injections that are painful or make them feel ill. The wonder is that they co-operate as well as they do, all things considered

Can this state of affairs be improved upon? There is no escape from the present situation until the goal which Ehrlich sought to reach over a quarter of

a century ago, the therapia sterilisans magna, is achieved, or until we come much closer to that goal than we are at present Chesney believes that we badly need better drugs for the treatment of syphilis, and we badly need a better understanding of how the arsenical and the bismuth preparations which we now have exert their action.

Among other administrative problems which might well be the subject of study, Chesney includes the determination of the best method of discovery of sources of infection, the determination of the best type of clinic management, and the determination of the most effective way to ascertain, periodically, the reliability of diagnostic laboratory services. All these questions are of immediate practical importance in any program of syphilis control and well deserve objective study and critical analysis.

Pathogenesis-The question of the rapidity with which Spirochaeta pallida invades the blood stream and the lymph nodes after syphilitic inoculation is of considerable theoretical and practical importance G W Severac³ conducted a series of experiments (1) To determine with some degree of precision the earliest instant at which the blood of a rabbit moculated with syphilis becomes infectious, (2) to determine the concentration and the amount of blood of a syphilitic rabbit necessary to produce infection when injected intratesticularly into a normal rabbit. (3) to determine whether the blood of the infected rabbits may not be rendered noninfectious by a suitable treatment

In order to produce syphilitic infection in rabbits an emulsion of Spirochaeta pallida of the Nichols strain was injected into both testicles of 16 rabbits. Active lesions containing spirochetes were observed in the testicles at the usual period

of from four to eight weeks. The blood of infected rabbits was then examined at various periods before the appearance of lesions and later, by the inoculation method. For this purpose whole blood usually in the amount of 0.5 cc. was again injected into one or both testicles of a normal rabbit. If no lesions appeared during a six-month period it was concluded that no spirochetes were present in the blood. The appearance of lesions containing spirochetes was considered evidence of the presence of spirochetes in the blood which was injected into the animal

The authors found that dilutions of from 1 10 to 1 10,000 failed to produce infection even when as much as 0 5 cc was injected into each testicle. Positive results were obtained only when whole blood or a 1 2 dilution was used, 0 1 cc (0 05 cc of whole blood) was sufficient to produce lesions in the inoculated rabbits. As a result of this finding, undiluted blood was used and the amount injected was 0 5 cc into each testicle.

Statistical data are given showing the interval elapsing between the infection of the rabbit and the appearance of spirochetes in the blood stream Following intratesticular inoculation with an emulsion of spirochaeta pallida, the blood was taken either from the ear or from the heart of the rabbit at various intervals of time, namely, 5, 10, 15, 30 minutes, 1, 5, 24, 48, and 72 hours, 1, 2, 3, 4. 5, 7, 10 weeks, 3 months, and 1 year after inoculation. These data show that the blood of the inoculated animal became intectious as early as five minutes after inoculation Previous investigators found that infectivity took place not later than seven days after moculation These data also show that the blood remains infectious in about 50 per cent of the animals as late as 6 months, 1 year, and $2\frac{1}{2}$ years after moculation, at which time the lesions

have disappeared These findings are not in agreement with the reports of Eberson and Engman and of McNamara that the blood is infectious only during the early stages of the infection

Statistical data are also given showing the results secured when the infected rabbits were treated with an intravenous injection of neoarsphenamine in doses of 0 040, 0 020 and 0 005 Gm per kilogram of body weight. Blood was taken 30 minutes after inoculation to determine the presence of spirochetes and also after treatment. In the cases studied (26) the blood was rendered noninfectious by treatment.

While the authors consider that their study proves that the blood is infective immediately after inoculation and long before the appearance of primary lesions, they suggest further study to establish the infectivity four or five months and longer after inoculation

In view of an increased incidence of syphilitic infections due to blood transfusion these experiments should be considered as a warning against reliance on the negativity of the Wassermann reaction alone. Some donors of blood may show a negative Wassermann test and no visible signs of syphilis because their infection is in the early seronegative stage. In others the infection may be in the latent stage when visible signs of syphilis are lacking and the Wassermann reaction is negative.

Unfortunately for comparison conditions for dissemination in experimental animals and man are probably not identical. There is reason to believe that spirochetes in man are limited to the chancre and neighboring glands during the seronegative primary stage, thus accounting for the better results from therapy as compared with therapy started in the seropositive primary stage.

Discussing the organism of syphilis J H Stokes4 refers to the extraordinary fitness of the Spirochaeta pallida for its human habitat, which Warthin rated as the most exquisite example of symbiosis in the pathogenic field Evidently we are dealing with a parasitic diplomat of extraordinary adaptability, an opportunist whose persistence in the anergic mouse now warns us of the human asymptomatic carrier and is beginning to arouse the misgivings of both laboratorians and clinicians Syphilologists are frankly puzzled by the patient who, with no recognizable source or onset, seems to have been a bearer of the disease through the larger part or all of a lifetime The anergic, hypergic, and hyperallergic states in tuberculosis are beginning to find parallels in syphilis Treatment refractoriness which many observers believe to be on the increase is a case in The theory of spirillicidal drug action has sidetracked our realization of what is now becoming increasingly apparent,-that all our antisyphilitic drugs act not alone by poisoning the organism direct but also by arousing the defense mechanism of the body no such defense can be effectively aroused by drugs (1 e, treatment resistance), we are confronted with a picture only too familiar already from typhoid to the virus diseases,—that of a treatment-refractory, infectious or relapsing carrier, the unknown X in the transmission and perpetuation of the disease. The more we study the defense of the once-infected individual against syphilis, the clearer becomes the definition and the seriousness of the anergic state Experimentally we know this to involve the persistence of the infecting agent indefinitely in full virulence as in the carrier mouse, with the possibility of change in tropism of the parasite by asymptomatic localization within the anergic animal, as in Raiziss' isolation of a strain of Spirochaeta pallida neurotropic for rabbits, from the brains of asymptomatic mice Since the anergic and hypergic states imply inaccessibility of the organism to the usual spontaneous bodily defense as well as to the usual resources of treatment, there may follow an inveterate predisposition of the untreated individual to infectious relapse instead of the usual spontaneous decline of infectiousness. Such a tendency may be prolonged over years Again, a strain of drug resistant organism may be, as Beerman's elaborate work suggests, a partial explanation of treatment-resistance Such strains may ultimately come to the front as the drug-susceptible ones are done away with, leaving us with a body or reservoir of infection with which present-day treatment cannot cope These problems of the spontaneously anergic and the treatment-refractory carrier with his recurring unrecognized relapses, together with that of the treatment-resistant strain of micro-organism, challenge the optimism of present-day chemotherapy

Prophylaxis—Three methods of preventing syphilis are discussed by J E Moore, namely, mechanical prophylaxis, chemical prophylaxis, and chemotherapeutic prophylaxis Mechanical prophylaxis is accomplished by means of the condom, which prevents the transmission of the infection by direct contact of moist genital surfaces in sexual intercourse Chemical prophylaxis may be accomplished by means of soap and water or by calomel ointment This method is best administered by an expert at a prophylactic station Chemotherapeutic prophylaxis includes the administration of drugs after the virus has penetrated the tissues It is best accomplished by intramuscular injection of bismuth and possibly stovarsol (acetarsone) by mouth

or arsphenamine by intravenous injec-It has been shown that syphilis may be prevented with a fair degree of certainty by intramuscular injections of bismuth given over an indefinite period of time This method, while applicable to certain groups of prostitutes, is not suitable for a general population. As to the solution of the problem, Moore states that it does not lie in the direction of mechanical prophylaxis He emphasizes the need of educating the layman to recognize the early symptoms of the disease and the bringing of all infectious cases under adequate treatment stresses also the need for improved standards of medicine and of educating all physicians to treat the disease by improved methods

Two possibilities which anticipate the infecting occasion and operate while intelligence still commands lie open for tuture study according to J H Stokes 6 There is a bit of hope in the direction of the bismuth 'plug," the injection or series of injections of the drug given to the professional disseminator of syphilis or the inveterate sampler of risks. The essentials, a planned intention which is against human nature, a period of preparation, the selection of effective salts, the duration of the protection, the question of the masking [of generallization and failure to prevent invasion by the Spirochaeta pallidal are all still obscure and controversial issues

Diagnosis—Adequate and universally available laboratory service for dark-field examinations is a first essential in the control of syphilis and the Advisory Committee to the United States Public Health Service^{6a} state that the importance of the dark-field examination in the diagnosis of syphilis should be impressed in every possible way upon all physicians, clinicians, and other workers interested in public health measures

directed against the venereal diseases State health departments should aim to place at the disposal of every interested physician or group two types of facilities: (a) The direct dark-field examination of secretions by a properly equipped laboratory administered as described above; and (b) indirect dark-field examinations (capillary-tube method) through the State laboratory.

Minimum requirements for direct dark-field examinations should be \cdot (a) A dark-field microscope of recent pattern, maintained, if possible, as a permanent set-up and not subjected to other uses, (b) the necessary slides, cover glasses, and other equipment, specifications for which should be prepared and furnished by the State laboratory with the co-operation of the Public Health Service, and (c) interpretation of each specimen submitted either by the laboratory director in person or by a medical or technical subordinate well trained in dark-field technic

Indirect dark-field examination by the capillary-tube method should be encouraged as a procedure of promise. The State laboratory should provide physicians with a standard mailing container for this type of dark-field examination. Directions for the collection of specimens by this method should also be enclosed in each package. Constant efforts should be made to inform the physician as to the technical details of specimen collection for the indirect dark-field method of diagnosis as well as to encourage him to use it.

Specimens in capillary tubes received in the laboratory of the State Health Department or private laboratory should be examined with the same promptitude accorded other emergency examinations because of the great importance of time in the effective diagnosis of seronegative primary syphilis. Provision should be

made for submission of dark-field reports by telegraph or telephone when desired Such reports should also be sent out by mail within 18 hours of receipt of the specimen in the laboratory. The equipment for the examination of indirect dark-field specimens and the qualifications of personnel entrusted with such examinations should be identical with those recommended for direct dark-field examination

According to R. A Vonderlehr⁷ a finding most important to physicians in private practice was the demonstration that spirochaeta pallida in serum remains viable and in most cases motile when transported as a specimen through the mails. Following the work of Mahoney and Bryant on the delayed dark-field examination, a number of health departments have adopted this procedure

It is well known that many physicians do not feel that they are thoroughly qualified to perform a dark-field exam-Furthermore, the occasional performance of such an examination by a physician in general practice would probably result in a larger number of errors in recognizing Spirochaeta pallida on a morphologic basis than would the regular performance by a competent laboratory worker of the same examination on a large scale. The delayed darkfield examination, therefore, not only makes it possible for the public health laboratory to extend diagnostic service to all physicians for their seronegative primary cases of syphilis but should also insure greater accuracy masmuch as all examinations can be made by an experienced technician

It has been suggested that in view of the high mortality rate of syphilis, tests for syphilis be performed routinely in the examination of all applicants for insurance C R Rein, M Le Moine and M G Stephens⁸ believe the Kline test

especially adaptable for insurance exammations because it gives results of maximum specificity and sensitivity. Sufficient blood for this test may be secured from the finger or ear lobe and sent in capillary tubes to the laboratory for testing The test can be performed in a small home office with a minimum equipment at a cost of about 20 cents including cost of materials and the technician's salary. One hundred or more tests can be performed in about two hours It is not necessary for the applicant to know the purpose of the test The Service Volume of the Cyclopedia of Medicine for 1937 reviewed the evaluation plan of the United States Public Health Service to appraise the various modifications of the complement fixation methods and called attention to the fact that the Kline Exclusion heated serum test was the most sensitive of the group which had less than one per cent false positives

The future of serology for the diagnosis of syphilis is an interesting subject for speculation II H Hazen judges from the present trend the flocculation tests will probably displace the complement fixation tests for the diagnosis of syphilis Where but little blood is available, as in infants, slide microscopic tests requiring but a few drops will be available Similai tests of great delicacy may also be used upon a small quantity of chancre fluid. It is possible that chancre serum will show a positive test while the blood serum is still negative For controlling treatment quantitative tests upon both the blood and spinal fluid will be employed In addition the majority of laboratories will perform tests with a specificity of well over 99 per cent and a sensitivity considerably greater than is usual at present The work of numerous serologists shows that this is perfectly feasible

It goes without saying that syphilis can often be diagnosed by other means than serologic It may be true that during the early eruptive period the serologic test is much the best confirmatory evidence that we possess, but in the early chancre the dark-field in skilled hands is infinitely better Here it is well to point out that the mouth contains spirochetes very similar to treponema pallidum. Parenthetically it may be remarked that it is conceivable that such organisms might be found upon other portions of the body, if only for a short time In late syphilis an x-ray study of the bones or aorta may be invaluable. In neurosyphilis there are other valuable tests upon the spinal fluid in addition to the serologic ones It has been the experience of Hazen that women who have been pregnant frequently show a negative blood serology In this class the history of repeated miscarriages, or the finding of a syphilitic placenta, are of the greatest aid. It should be distinctly understood that Hazen feels that every pregnant woman should have her blood examined for syphilis, preferably during an early period. These few examples by no means complete the list but they should suffice to show that serologic study is not the only way to diagnose syphilis. As is invariably the rule a laboratory procedure is a good servant but a bad master

Importance of a Routine Wassermann Test in Private Practice—In discussing this question M P Warner and B W Warner¹⁰ offer the following conclusions

"There is an active, concerted attempt on the part of health authorities to eradicate syphilis. The health authorities are stressing the need and importance of clinic and hospital facilities for the task. Only recently are hospitals recognizing the importance of routine serologic tests

in all of their outpatient and inpatient departments. It is believed that only by diagnosing the individual case will syphilis be controlled and the incidence materially reduced.

"Many of the authorities are uncompromising and impatient in their criticism of the rôle of the private practitioner. Much of this criticism is deserving The physician must become more syphilis conscious, his "index of suspicion" must be raised, and the Wassermann test must occupy the same place in a routine medical examination as taking temperature or a urine analysis

"Let us not, as private practitioners, wait until we are régimented into the plan for syphilis control, but let us rather voluntarily enlist and expand our In recognizing and healing services syphilis we are diagnosing and curing the patient and acting further as individual health officers in the broader scheme of public health. We are consulted in confidence and privacy by the distracted and unfortunate patient who is afflicted with venereal disease With co-operation of the public health facilities we can render efficient, satisfactory service"

Prognosis - Efficacy of Natural Curative Processes-Syphilis is essentially a chronic disease. The value of high temperatures in destroying the spirochete has been widely discussed in recent years F Jahnel¹¹ believes that hibernation will cure syphilis in the animal, basing his conclusions on experiments carried out on the rell-mouse, an animal that hibernates seven months year in a lethargic state with decreased metabolism and a markedly lowered body temperature, which approximates that of the environment Jahnel kept syphilitic rell-mice throughout the winter sleep, then inoculated rabbits with their organs and brains

with negative result. The syphilitic infection seemed to disappear during hibernation and Jahnel asks why it would not be possible to affect syphilis in human beings as favorably by lowering the temperature as one can by inducing fever.

The cure of congenital syphilis during bodily growth is evidence that there are many natural factors which favorably affect syphilis. Of particular interest in this connection is the striking observation that the female sex, despite equal infestation with syphilis, is afflicted with paresis to a much less degree than the male sex, an observation which many authors ascribe to the protective action of pregnancy

J E Kemp, 12 studying the effect of pregnancy on the course of syphilis in experimental animals, feels that while pregnancy exerts an appreciable inhibiting effect upon the course of syphilitic infection, it is not the only factor responsible for the altered course of the disease in the female. The experiences of Frazier and his colleagues in the treatment of experimental rabbit syphilis with estrogenic substance prepared from pregnancy urine suggests that this hormone might be responsible for the modified course of the infection in the pregnant temale. With this Kemp does not agree Further experimental and clinical studies are necessary before the relationship of sex and pregnancy to the course of syphilitic infection can be accurately determined

Treatment—Treatment as a Factor in the Control of Syphilis—The aims of treatment in early syphilis are first, the prevention of transmission of the disease by treatment and, second, the cure of the individual patient J E Moore¹³ believes there are compelling reasons for the adoption of a standard method of treatment by clinics

and practitioners throughout the country which he summarizes as follows

- 1. The average patient with early syphilis is a healthy young adult, free from complicating diseases
- 2 The manifestations of the disease and the extent of involvement of important body structures are surprisingly uniform
- 3 The response of patients to treatment is equally surprisingly uniform
- 4 The evaluation of the worth of any treatment method requires years of study by experts, and is beyond the capabilities of the average physician
- 5 An evaluation of treatment methods by two independent agencies, the co-operative clinical group in co-operation with the United States Public Health Service, and the League of Nations health inquiry, has definitely established the worth of certain broad principles, deviation from which (until better methods are developed) constitutes a confession of ignorance or incompetence

These principles are

- (a) Treatment must be continuous No rest period of any kind until treatment is finished
- (b) Treatment must be prolonged to a minimum of 15 to 18 months, regardless of seronegativity or seropositivity at the time treatment is begun, and regardless of serologic progress during treatment
- (c) For the control of infectious relapse, a minimum of 20 injections (each) of an *arsphenamine* and a *heavy metal* are essential
- (d) For the accomplishment of individual cure, a minimum of 30 injections of an arsphenamine and 40 of a heavy metal are desirable
- (e) Lifelong post-treatment observation with periodic re-examination is essential to determine the fact of cure

An outline of treatment which fulfills these qualifications has been proposed by the co-operative clinical group, on the basis of a study of more than 6000 patients with early syphilis. This treatment plan should be adopted without change by clinics and practitioners the country over and should be adhered to as to choice of drugs, dosage, continuity, and duration, until it is definitely proved by the independent studies of several different observers that other drugs, different methods, or shorter duration of treatment produce superior results

It is true that present treatment methods, both of early and late syphilis, are unsatisfactory in the sense that treatment is too uncertain in outcome, too prolonged, too expensive, and too dangerous, and that continued experimentation to develop better, more rapid, cheaper, and safer methods should con-Nevertheless, the premature adoption by the medical profession as a whole, and by health department syphilis clinics in particular, of unproved drugs new methods of administration of already known drugs, or new nonspecific methods of treatment, should be discouraged until the passage of time has by proof and independent confirmation from several expert sources removed such methods from the realm of experimentation to that of practicability

Oral Administration of Bismuth—
The recognized method of giving bismuth today is the intramuscular injection. The oral administration, however, has been investigated and was discussed in the Cyclopedia of Medicine Service Volume (p. 241) in 1937. It was then decided that further clinical experimentation was necessary before arriving at any conclusion as to the value of orally administered bismuth C. C. Thomas 14 found as a result of

further investigation of this problem that conventional intramuscular bismuth therapy was markedly superior to peroral administration and was unable to confirm the favorable reports of Serefis and Mulzer on the efficacy of oral bismuth administration as determined by sterilization and healing of early infectious syphilitic lesions or effects on serologic tests

Oral Medication for Syphilis — Commenting editorially on this subject J E Moore¹⁵ reviews briefly the experimental and clinical background of the drugs proposed for oral administration in the treatment of syphilis in order to determine their place in present-day syphilis therapy

The arsenical preparation most widely used orally in this country and abroad is the *sodium salt of 3-acetylamino-4-hydroxyphenylarsonic acid*, known variously as *stovarsol* (France), *spiro-cide* (Germany), or *acetarsone* (United States)

In human beings and in acquired syphilis, the oral use of acetarsone, whether for prophylaxis or treatment, has been chiefly limited to France and Germany, more especially the former, and as nearly as can be determined from the literature, it has met with sufficiently small success as to have been almost abandoned in both countries It has never been used for this purpose on any large scale in the United States Surprisingly enough, however, acetarsone has been used by many pediatricians in this country in the treatment of infantile congenital syphilis, and the reports of its therapeutic efficacy in this condition, so far as healing of lesions and serologic reversal are concerned, are almost uniformly enthusiastic Sufficient time for long term clinical evidence of "cure," comparable with arsphenamine-bismuth data, has not as

yet elapsed Theoretically, the oral use of acetarsone in infantile congenital This form syphilis is to be deplored of congenital syphilis is entirely analogous as to treatment response with acquired primary and secondary syphilis, i e, it is curable, probably in the biologic sense of eradication of the last remaining treponeme, as well as in the symptomatic sense of healing of lesions and prevention of relapse, and the serologic sense of permanent serologic negativity This cure has been amply demonstrated to be capable of accomplishment with standard methods of treatment, as in early acquired syphilis, with an arsphenamine product and bismuth However sympathetic one may be with the desire of parents and physicians to find a method of treating infants less painful and disagreeable than "needles," one cannot escape the feeling that in infantile congenital syphilis the substitution of acetarsone for older proved methods offers a serious uncertainty of ultimate clinical outcome instead of a practical certainty, and that the use of the drug under these circumstances, and in view of its uncertainties in experimental animals, is hardly justified

As matters stand at present, acetarsone by mouth has no proper place in the treatment of syphilis in human beings unless on a purely experimental basis. If such experimentation on men, without adequate previous evidence of the value of the drug in experimental animals, is justified at all, it should be limited to patients with late syphilis, congenital or acquired, in whom radical cure is impossible, and in whom symptomatic relief and the prevention of relapse are the sole desiderata

The other preparations that have been suggested for the oral treatment of syphilis are several of the compounds of bismuth—potassium bismuth tar-

trate, sodium bismuthate, and bismutrate. The experimental background of potassium bismuth tartrate is at present unconfirmed, and there is no evidence that it is of value in the treatment of human syphilis Sodium bismuthate is still in the period of experimental study and, at present, cannot be evaluated Bismutrate, however, has attracted attention because of the studies of Serefis and Mulzer

There is a growing tendency to disregard Ehrlich's insistence that careful and exhaustive animal experimentation. the results of which can be translated with a great degree of certainty to man. must precede the introduction of new drugs in the treatment of human syphilis. Continued disregard of this principle is obviously dangerous, since it may easily be followed by the appearance on the market of innumerable preparations for oral administration which have no place or value in the treatment of syphilis Since inferior drugs, treatment schemes, etc. are ultimately accurately evaluated as time passes and are either discarded altogether or are assigned to a small sphere of usefulness, the above consideration is one which will eventually be adjusted A much more serious danger, it thorough experimental testing in animals does not precede the introduction of new drugs for the treatment of syphilis, follows the attempts to evaluate them by treating syphilis in man This can be done satisfactorily only in individuals with primary and secondary syphilis, and. therefore, new preparations are identified with the satisfactory results which follow their use in the treatment of early syphilis The danger of this is obvious There are still a large number of physicians treating syphilis who are unaware of the background of the accepted schemes for the treatment of early syphilis If an investigator, therefore.

presents favorable results following the oral use of a drug in the treatment of early syphilis, his protest that it should not be used in this stage of the disease is to these physicians a scientific altruism not substantiated by the very evident merits of the drug

It is felt by many that there is little place at present for new drugs in the treatment of syphilis unless they show promise of superiority to the most efficient of those in use at the present time This does not mean that efforts to evolve new preparations, whereby the treatment of syphilis would become shorter, less expensive, and more convenient, should However, before any not continue preparation is offered for general use in the treatment of syphilis, no matter how it is to be administered, it must be preceded by the same careful experimental and clinical study which preceded the introduction of arsphenamine There is insufficient evidence that the drugs proposed for the oral treatment of syphilis have met these requirements

New Arsphenamine Synthetics in the Treatment of Syphilis-There are outstanding obstacles to adequate clinical testing of drugs to be used in the treatment of syphilis J H Stokes and H Beerman¹⁶ believe the most important of these to be sales organization influence, excessive costs, both in money and in time, of research in this field. a disposition on the part of the manufacturer to save by madequate clinical testing and to rush drugs prematurely to the market, incomparability of the therapeutic index in animals and man, inadequate contact between clinician and laboratorian, excessively distrustful attitude toward manufacturer on the part of clinical and scientific authority, lack of controlled and defined procedure in clinical as well as laboratory testing, nonrecognition and noncontrol of personal equation elements which are inevitably operative, and disposition to overexpand so as to cover all variations of syphilis rather than to define or evaluate the field of usefulness of a drug

In particular, sharp criticism was directed against the practice of distribution of samples to inexperienced and scattered practitioners, which, while it swells the total number of injections of a drug, provides little in the way of effective and responsible evaluation

The clinical head of a testing organization was advised to distrust or refuse participation in clinical study (a) when sales organization and propaganda are in evidence, (b) when direct contact with the head of the manufacturer's scientific organization cannot be had, (c) when no adequate information is given as to results of tests on animals, (d) when frequent conference, preferably personal, is not possible; (e) when the clinical material available is not suitable or is too small to permit adequate control observations or reports within a reasonable time

The clinical tester of antisyphilitic drugs should, they say, accept for test only drugs for which he has the proper material in sufficient quantity should have, in addition, a laboratory equipped for making controlled serologic and dark-field examinations. assistants with adequate experience, an effective follow-up service, and a treatment organization which maintains constant technical performance and reaction incidence. If possible, there should be a single responsible head for the investiga-Further, experience with triarsen indicated the need for a weekly quantitative serologic test for all patients to provide the basis for controlled serologic evaluation

The clinical evaluation of an antisyphilitic drug having been undertaken,

it should, according to these authors, seek to establish (1) the nonexistence of harmful by-effects not identified in tests on animals, (2) the spirillicidal value of the drug in man, no matter what may be the field of treatment for which it is proposed, (3) the incidence of therapeutic shock or Herxheimer effect, (4) the rate of healing of lesions, (5) the symptomatic response of various structures, (6) constitutional effects, (7) the effect on the serologic reaction of the blood, (8) the incidence of clinical and serologic relapse. (9) the reaction and response of the spinal fluid, (10) the evidence of therapeutic paradox, (11) the response and evidence of injury to special organ systems, and (12) the value of the drug in cardiovascular syphilis, neurosyphilis, pregnancy, and interstitial keratitis

The authors continue their extensive article with a discussion of a new drug, tharsen, a new arsphenamine which appears to satisfy the demands of the Cooperative Clinical Group and the International Committee (League of Nations) for the treatment of early syphilis

J E Moore and his co-editors¹⁷ object to the term arsphenamine synthetic. The word arsphenamine was coincid to designate the synthetic compound 3-3-diamino-4-4 dihydroxy arsenobenzol and to include all its various salts. The term arsphenamine has by usage come to include all of the closely related arsenobenzol derivatives. Arsphenamine synthetic has, however, no basis in usage, and etymologically it is meaningless.

Postarsphenamine Jaundice — Because of the widespread use of arsenical compounds in the treatment of syphilis, the problem of postarsphenamine jaundice today assumes considerable importance. The subject is thoroughly dis-

cussed by L $\,$ J $\,$ Soffer¹⁸ and summarized as follows

A total of 18,250 patients received antisyphilitic treatment in the Johns Hopkins Hospital from 1919 to 1934, inclusive Of these, 158 developed jaundice, an incidence of 087 per cent

Arsphenamine causes jaundice one and one-half times as frequently as neoarsphenamine, while tryparsamide shows the lowest incidence of treatment icterus

The percentage incidence of postarsphenamine jaundice is almost three times as great among the white patients as among the colored patients

The stage of the disease during which the patient received antisyphilitic treatment bears no relationship to the frequency of postarsphenamine jaundice

Sixty-eight per cent of the cases of postarsphenamine jaundice seen in Johns Hopkins clinic occurred during or after the completion of the first ten intravenous arsenical treatments

There is no relationship between the total amount of drug used and the development of jaundice

The time relationship of the appearance of jaundice to the last arsenical injection was determined in 143 cases seen at Johns Hopkins clinic. In 295 per cent, jaundice appeared one to three days after the last injection. In 535 per cent it occurred within ten days. Thus, in a little over half, jaundice occurred early, while in the remainder the reaction may be spoken of as being "delayed."

The hypotheses concerning the phenomenon of "delayed" postarsphenamine jaundice are discussed

The relationship of the rôle of heavy metal to the development of jaundice is difficult to determine. In Soffer's series there were two instances of jaundice following the use of bismuth subsalicy-late. Neither of these patients had ever received arsenical therapy. In one

instance the icterus appeared two days after the last injection and in the other instance a month elapsed before the appearance of jaundice

The clinical course of postarsphenamine jaundice is described The frequency of the occurrence of various symptoms is presented, the most common being malaise, nausea, and vomiting These symptoms usually appeared four to eight days before the appearance of Enlargement of the liver occurred in about half the cases, the liver descending from one to nine fingerbreadths below the right costal margin In seven instances the spleen was slightly enlarged, and ascites appeared in four cases. The presence of marked fever in the absence of any other obvious cause suggests the possible development of either arsphenamine dermatitis or the presence of an extensive necrotic process in the liver

Complete blood studies were made on 32 patients with arsphenamine jaundice who were hospitalized Fifty per cent of this group had a slight secondary anemia Whether this was due to the arsenical icterus or to syphilis per se could not be determined White cell counts and differential studies were usually normal in the uncomplicated cases, whereas, when the icterus was associated with a dermatitis, there generally was present leukocytosis with an increase in the eosino-Those patients philes and monocytes who developed acute yellow atrophy of the liver had a leukocytosis with relatively no change in the differential studies

The duration of jaundice was carefully observed in 105 instances. The duration varied from 10 to 100 days. In 74 cases the interus lasted from 25 to 35 days.

Eighty-one of our patients received further arsenical treatment after the

icterus had subsided Of this group, two eventually developed another attack of jaundice.

Of 158 cases of arsenical hepatitis, 10, or 63 per cent, developed acute yellow atrophy of the liver. The incidence of this complication was considerably greater in women than in men and in instances of late syphilis than in early cases.

Of 158 cases of arsphenamine jaundice, there were 16 instances, or ten per cent, of an associated dermatitis. In 11 of the 16 patients, the drug used was arsphenamine, in four, neoarsphenamine, and in one, tryparsamide. Five of the 16 patients received subsequent further treatment with an arsenical. One of these patients again developed jaundice, while none of this group had a recurrence of the dermatitis

The ultimate prognosis of patients with postarsphenamine jaundice is discussed, and the statement made that "the available evidence certainly suggests that the long continued use of arsenical compounds may produce progressive damage to the liver"

The Treatment of Syphilis as Understood Today — In an excellent paper on the control of syphilis with a critical examination of some of its problems, J H Stokes¹⁹ summarizes what we now definitely know we can do with existing drugs and methods in controlling the course and transmission of syphilis He confines himself to a summary of the American phase of the investigation published under the names of the CCG or Co-operative Clinical Group and the United States Public Health Service This summary is of sufficient value to warrant its inclusion verbatim

Early and Latent Syphilis—1 Relapse in all forms occurs in early syphilis in 101 per cent in the aggregate Relapse in all forms occurs in early syphilis in 197 per cent if observed six months or more

Infectious (mucocutaneous) relapse occurs in 12 l per cent of a six months' observation material, six per cent in all cases

- 2 Seropositive primary syphilis has the highest incidence of mucocutaneous relapse (95 per cent versus 47 per cent for secondary, 83 per cent for seronegative primary syphilis
- 3 Ninety-one per cent of infectious relapse occurs in the first two years
- 4 Half of all relapse lesions are infectious, and two-thirds of them occur on the penis and vulva
- 5 The more arsphenamine the less relapse

9 injections or less—7 7 per cent 10 to 19 injections—4 0 per cent

20 to 29 injections—3 6 per cent

30 to 39 injections—1 2 per cent

The critical point is between the fifth and the ninth injection. Of those who received only one to four arsphenamine injections, 64 per cent relapsed, 10 per cent infectiously of those receiving five to nine injections, only 14 per cent relapsed.

- 6 Much arsphenamine and little heavy metal gives one-half the relapse that little arsphenamine and much heavy metal does (27 per cent versus 53 per cent)
- 7 Bismuth is more effective than mercury arsphenamine-mercury therapy gives 96 per cent mucocutaneous relapse as compared with only 36 per cent under arsphenamine-bismuth therapy
- 8 Satisfactory results ("cures") are now being attained in 527 per cent of cases of early syphilis in the aggregate, irrespective of the amount and method of treatment
- 9 Seronegative primary syphilis, yields 86.4 per cent of "cures" in 2 to 20 years' observation by a continuous

- (no rest interval) system of combined arsenical and heavy metal treatment
- 10 The proportion of "cures" by the same method falls to 643 per cent in seropositive primary cases
- 11 It rises again to 815 per cent when treatment is begun in the secondary stage by a continuous system.
- 12 Even with totally irregular treatment, 547 per cent curative results can be obtained in seronegative primary syphilis
- 13 In seronegative primary syphilis, the highest proportion of curative results is obtained with 10 to 19 arsenical injections with heavy metal, in seropositive primary syphilis, with 25 to 35 injections, in secondary syphilis, with 20 to 29 injections
- 14 Seropositive primary syphilis, on which for a long time, even with improved education of doctor and patient, diagnosis and treatment will tend to concentrate, has the poorest outlook of all stages, with respect to relapse and cure, by continuous treatment (otherwise the most efficient system)
- 15 There is definite evidence that full arsphenamine dosage is more effective than overcautious or reduced dosage
- 16 Try at least to pass the 20 mark with the arsphenamine and its accompanying heavy metal the results are substantially better
- 17 The resistant patient should receive further arsphenanine—at least ten more injections than the optimum for his stage—not heavy metal alone
- 18 The "refractory residue" of all systems of treatment ranges from 4 to 27 per cent, depending on technic (continuous, intermittent, irregular)
- 19 Continuous treatment (without rest periods) is more effective than intermittent treatment. The two systems, however, can be made to approach each

other by judicious selection of dosage and interval.

- (a) League of Nations results Relapse by continuous treatment, 082 per cent, by intermittent, 566 per cent (corrected for shortened observation).
- (b) American results—two to ten-year observation: "Cures" by continuous treatment, 80 per cent, by intermittent, 65 per cent
- (c) American results reinterpreted after the third month of treatment. A rest period of one month in the first year reduces the negative blood Wassermanns at the end of the year from 68 to 40 per cent. The delays in attaining seronegativeness are doubled (236 versus 116 per cent.) The fixed positives are trebled by intermittent treatment (6 per cent continuous, 18 per cent intermittent.)
- 20 Continuous treatment produces no more serious reactions than intermittent—18 per 1000 injections continuous technic, 19 per cent intermittent. For the heavy metal factor, which increases the tendency to reaction, the incidence was 085 per 1000 injections for continuous, 088 per 1000 for intermittent (3 to 12 months two-year observation basis)
- 21 So effective is modern treatment for early syphilis that the following statements are possible
- (a) In early syphilis, 32 doses of an arsphenamine with appropriate heavy metal in 65 weeks by continuous, or 21 months by intermittent technic, give, by the former 11 per cent clinical and 56 per cent serologic relapse in two to ten vears, by the latter, 42 per cent clinical and 75 per cent serologic relapse in the same period. With irregular and inadequate treatment, clinical relapse is 127 per cent, serologic 132 per cent. This includes the spinal fluid.
- (b) The American statistics reworked to compare with Bruusgaard's untreated

series show that in a 3 to 20 year observation 77 to 63 per cent of treated patients are Wassermann negative and symptom-free as compared with 24 to 33 per cent without treatment Adequate treatment by an effective technic gives 96 per cent symptom-free patients in three to ten years, no treatment, 61 per cent In 10 to 20 years, adequate treatment gives 74 per cent, no treatment 50 per cent.

22. The optimum treatment of latent syphilis consists of one year of continuous and a second year of intermittent treatment (a total of 24 arsphenamine injections and 50 to 60 doses of bismuth), subject to considerations of age, sexual activity, and other complications Continuous treatment the first year is essential for best results.

Cardiovascular Syphilis — 1 Cardiovascular syphilis developed in 16 per cent of 935 early syphilis patients followed from three to ten years, in 67 per cent of 105 patients in 10 to 20 years, but not one who had had adequate treatment for early syphilis developed a serious cardiovascular lesion in the 3 to 20 year group.

- 2 Adequate treatment improved the outlook of those followed one year after developing uncomplicated *syphilitic aortitis*, and prolonged the life of those who died, from an average span of 34 months to 85 months
- 3 Of patients adequately treated after detection of their *aortitis*, 63 per cent were found to be living, symptom-free, and arrested, of those inadequately treated, 40 per cent
- 4 Small arsenical dosage prolonged life 20 months longer than large
- 5 Preparatory heavy metal treatment is advised

Syphilis in Pregnancy — 1 Mother scronegative before pregnancy, 74 per cent apparently healthy children

Mother seropositive before pregnancy, 61 per cent apparently healthy children

2 Mother seronegative during pregnancy, 81 per cent apparently healthy children

Mother *seropositive during* pregnancy, 57 per cent apparently healthy children

Treated — 1 Seventy-eight per cent healthy children when treatment is begun before the fifth month

- 2 Sixty-one per cent healthy children when treatment is begun after the fifth month
- 3 Ninety-one per cent healthy children when ten arsenical and ten heavy metal injections were given before the fifth month
- 4 With *much* arsphenamine and *little* heavy metal *before* the fifth month, 85 per cent healthy children

With little arsphenamine and much heavy metal before the fifth month, 75 per cent healthy children

With much arsphenamine and little heavy metal after the fifth month, 55 per cent healthy children

- 5 Hence give the pregnant woman more arsphenamme, at least ten injections, beginning before fifth month. Add ten injections of heavy metal (bismuth)
- 6 Habitually aborting syphilitic women (two to three abortions each) produce seemingly healthy children in 69 to 78 per cent after treatment
- 7 The pregnant syphilitic woman tolerates arsenicals much better than the nonpregnant syphilitic woman (one-half as much dermatitis and one-fifth as much jaundice)
- 8 Untreated seronegative pregnant women—28 per cent healthy children

Treated in a previous but not present pregnancy—62 per cent healthy children

Five times as many miscarriages in untreated as treated

9 Hence treat every syphilitic woman early and adequately in every pregnancy

whether Wassermann positive or negative

10 The adequately treated syphilitic woman may not be, but the untreated syphilitic woman certainly is, a potential carrier of infection for the fetus up to 10 or 11 years after she acquires the disease

The 30-0-60-3 Formula—30 arsphenamine (or neoarsphenamine) injections

0 rest intervals

60 bismuth injections (insoluble)

3 years of treatment and observation

Try to keep treatment uninterrupted month after month, for at least the first six months to one year following infection. Every week of continuous treatment is vital at the start

Fixed positive blood Wassermann and Kahn tests, and relapses in the nervous system, together with prolonged infectiousness due to mucous membrane and genital recurrences, result from disregard of this principle

The Continuous Method of Treatment of Early Syphilis — If early syphilis is properly treated late syphilis will almost, even if not quite, disappear That early syphilis is not being properly treated is obvious from the fact that late syphilis is not disappearing, according to J E Moore ²⁰ On the contrary, in every urban American community syphilis heads the list of reportable communicable diseases and of the cases reported more than half are late cases

The spread of syphilitic infection may best be controlled by the elimination of the infectious patient. Arsphenamine is necessary to prevent infectious relapse—heavy metal alone does not suffice, less than four injections of an arsphenamine permits relapse in the astonishingly high total of 45 per cent, an incidence probably even higher than would occur if no treatment were given (though data on this form of relapse in untreated syphilis are lacking), at least 20 injections of

an arsphenamine are the absolute minimum required really to eliminate infectious relapse. The practical abolition of infectious relapse is related not only to the total amount of treatment given but also to its type. It is important to emphasize, however, that the public health aim of treatment and the end sought for the individual patient, require a type and total amount of treatment not very different for the one than for the other.

To concentrate now on the question of treatment, it is readily apparent that the failure of physicians as a group is due in small part to technical ineptitude, and in large part to the persistence of empiricism. There are a few simple principles applicable to the treatment of early syphilis, all of which are backed by sound experimental and clinical evidence. These are

- 1 Successful treatment depends on early diagnosis
- 2 The choice of drugs is limited to the arsenicals represented in the arsphenamine group, and to bismuth
- 3 Treatment should be continuous from start to finish, $i\ e$, without rest periods of any sort
- 4 Treatment must be prolonged to a minimum of (depending on the stage of infection) 12 to 18 months
- 5 Determination of "cure" requires lifelong post-treatment observation

In summarizing, Moore says that though the adequate treatment of early syphilis is of importance from the standpoints of the individual patient, of the public health, and of the public expense, and though proved adequate treatment methods are available, they are not being generally applied

The reason for this failure lies in part in the biology of syphilitic infection, i e, in the fact that it is sometimes, perhaps often, symptomless in the early stages,

in part in lack of knowledge of the laity of the prevalence, characteristics, and public and individual importance of syphilitic infection; in part in the failure of the medical profession to employ adequate methods of early diagnosis and treatment. Remedies for these three faults are briefly suggested The modern treatment of early syphilis is based on the five fundamental principles listed above.

Syphilis in Pregnancy

Untreated pregnant syphilitic women will give birth to diseased children four times out of five Congenital syphilis may be prevented with almost absolute certainty if beginning not later than the fifth month of pregnancy, the syphilitic mother receives a minimum of 20 weeks of continuous treatment with an arsphenamine and a heavy metal given concurrently or in alternate courses S S Paley²¹ studied the outcome of 617 pregnancies in women with syphilis who were seen at the Central Harlem Health Center between 1930 and 1936, and demonstrated that the outcome of the pregnancy is related to the amount of the treatment which the mother receives Syphilitic tragedies during pregnancy (the term Paley uses to include all untoward eventualities which prenatal syphilis may produce) occurred for 46 per cent of the women who received less than four injections of an arsenical plus heavy metal, but for only 27 per cent of those who received four to seven injections and for only 14 per cent of those who received eight or more injections According to J. E Moore22 four distinct steps are essential with the mutual efforts of the public health authority, the social and medical organizations devoted to maternal and child welfare and the medical profession as a whole These are

- 1 The adoption of a routine serologic test for syphilis in every pregnant woman by every prenatal and obstetric clinic, every physician, and every midwife in the country. This is obligatory that syphilis may be recognized.
- 2 Systematic education of women to report to physicians or prenatal clinics for prenatal care earlier in pregnancy than is now the average case. This is obligatory that treatment of the pregnant syphilitic mother may be started early enough to ensure a healthy baby.
- 3 Elimination of the delay of many days or weeks which now often occurs between the diagnosis of syphilis and the institution of treatment in pregnant syphilitic women. This is obligatory to ensure a healthy baby
- 4 Better application by physicians of the several methods of recognizing the presence or absence of congenital syphilis in the infant-cord Wassermann, x-ray, pediatric, and serologic follow-up, especially intensive in the first few months of life. This is obligatory that when treatment of the mother has failed to protect the child through failure of diagnosis, delay in starting or neglect of treatment the syphilitic baby shall be given the excellent chance of cure which early adequate treatment provides

The stamping out of congenital syphilis is an easy accomplishment compared with the elimination of the acquired intection. Every syphilitic baby is a failure of maternal education, of the public health authority, and of the medical profession, which should cause us all to blush with shame. Congenital syphilis must go, and must go quickly!

Syphilis and Unemployment

Recently medical directors of certain large industrial corporations and certain branches of the Federal Government have begun to require routine blood tests of all applicants for positions, have refused employment to those whose serologic reactions were positive, and in some instances have dismissed individuals already employed who were tested and found to have positive serologic Certain corporation medical reactions directors and lay officials assign several reasons for this policy The danger of transmission of syphilis to others by food handlers, etc., the risk that a syphilitic person handling machinery may endanger the lives of others, and the additional economic risk imposed upon the company by the possibility that the syphilitic individual may become disabled directly or indirectly because of his syphilis, thus imposing through various forms of industrial compensation or other types of social insurance the burden of his care upon the company or the Federal Government

According to J E Moore,23 these arguments for the use of the routine blood test as a standard for employment are not reliable. The danger of transmission of syphilis through nonsexual contact is slight even in the case of food handlers, barbers, and "beauticians" Even in these cases, if the patient begins treatment he becomes noninfectious, and remains so if treatment is continued 40 weeks. A much better policy would be for the employer to continue to employ the infected person contingent upon his beginning treatment and continuing it If the employee has late syphilis of more than five years' duration, there is no danger of his infecting his co-workers Furthermore the blood serologic test is not a criterion of infectiousness During the seronegative primary stage or during infectious secondary relapse, the test may be negative, though the patient is highly infectious for others The routine posi-

tive blood test cannot be used as a guide to infectiousness in industrial medicine

From the standpoint of public safety the risk that a syphilitic person handling dangerous machinery may endanger the lives of others is limited to patients with cardiovascular syphilis, neurosyphilis, or No evidence is available in paralysis medical literature which shows that industrial accidents are more frequently due to the carelessness of syphilitic persons (excluding the exceptions mentioned above) than are due to the carelessness of nonsyphilitic persons. Diagnosis of cardiovascular or neurosyphilis is not established by the routine blood test but requires a complete study of the patient Furthermore the public safety is not protected by the employment of nonsyphilitic persons unless these persons remain nonsyphilitic during the entire period of their hazardous occupa-Employment should be granted or continued provided adequate treatment has been or can be given

The greatest objection raised against the employment of syphilitic persons is that an economic risk is imposed upon the company by industrial compensation or other forms of social insurance. Data are not available to support this statement

The present trend toward unemployment of syphilitic persons, if continued, may lead to a serious social situation. About 12,000,000 people in the United States have *syphilis*. About one-half of these now have and will continue to have positive serologic tests whether or not they have adequate treatment. The Federal Government and large employers will soon be confronted with many problems and questions regarding the providing of work for the syphilitic indivual. If these 12,000,000 people are

thrown out of employment, there will be a heavy tax burden for caring for them on the relief rolls. Moore believes that the problem can be worked out in a more intelligent and satisfactory manner.

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THE TEETH

By CONRAD F. HELLWEGE, DDS

Dental Caries

Clinical observation reveals that the activity of dental caries varies throughout the different periods of life

Dental caries is primarily a childhood disease After this time it becomes less and less active and in many persons ceases entirely In some persons, however, the condition again becomes active after 50 or 60 years of age Charles F Bodecker, 1 Columbia University, indicates that the concept of dental caries is changing, the old view being that destruction of the teeth was due solely to food This, however, retention and bacteria is giving way to a more complex con-For example, ception of the problem the fact that an increased vitamine D content in the diet of children reduces the activity of dental caries indicates that systemic conditions, either by way of saliva or dental pulp, or both, affect the welfare of the teeth

Dental caries are classified into three groups

- 1 Acute crown caries, affecting principally children and young adults. Acute dental crown caries affects first the enamel fissures or faults of the maxillary and mandibular molars and premolars, later the approximal surface of these teeth, then the maxillary incisors and lastly the anterior mandibular teeth.
- 2 Chronic dental caries, found usually in middle aged individuals affects the various surfaces of the teeth in the same order as that of the acute type, but the severity is slower. This type from the very beginning is a slow, destructive process
- 3 Acute dental root caries usually affects the teeth of persons past middle age. Here the crowns are often either

completely noncarious, or at most have small occlusal fillings. These lesions affect the roots of the teeth, usually at the interproximal surfaces, food impaction seems to be the external cause. The penetration varies in rapidity, being greater than that of the chronic type and somewhat slower than the acute crown caries

The clinically observed variations in the activity of dental caries seems to be influenced by

- 1 Systemic conditions A disturbance of some phase of the calcium-phosphorus-vitamin D complex appears to increase the activity of dental caries
 - 2 Character and location of the lesions
- 3 Change in the permeability of the teeth. The comparatively high permeability of recently erupted teeth allows the external destructive force, acid, to penetrate rapidly, resulting in acute dental caries. The lowered permeability of matured teeth is a barrier to this attacking force and chronic dental caries is therefore a slow, destructive process.

Leukoplakia

S William Becker,² University of Chicago, gives a review of the leukoplakia problem as related to the mouth

Mucous membranes react to chronic irritations in a characteristic manner, resulting in the formation of white patches known as leukoplakia. At first the lesion presents a red granular and slightly sensitive area, gradually becoming whitish gray. Upon continued irritation a bluish white plaque develops, tightly adherent and having the appearance of being pasted on the mucous membrane. When this area becomes thickened and warts an ulcer may appear, which is some-

times a sign of malignancy Leukoplakia occurs most commonly in men, past The inner surface of the middle life checks, the tongue, hard palate and gums are the areas most frequently involved The causes are local irritation and syphi-The lesions due to local irritation are at the site of irritation and may be the result of a smoker's pipe, chewing tobacco, natural or artificial teeth in malocclusion, badly fitting plates and bridges, Lesions due to syphilis are commonly on the tongue and at the oral commissures The lesions must be differentiated from those of Fordyce's disease, lichen planus, lupus erythematosis, psoriasis, oral thrush, canker sores and syphilitic mucous patches

The change is essentially in the epithelium, which has a great tendency to become malignant squamous-cell cancer

Treatment must destroy the epithelium, resulting in a scar, which will not become malignant. The *electric cautery* is the treatment of choice.

Allergic Manifestations in the Oral Mucosa

The clinical findings in allergic phenomena of the mucosa with details of detection, clinical characteristics, differential diagnosis and the method of desensitization have been discussed by Cleveland J. White 3

Twenty-two cases were studied in the past three years in which the allergens were detected. Allergic manifestations can be caused by the ingestion of foods or medicaments (ingestants), by breathing in certain materials (inhalants) and by contact with extraneous substances (contactants). Allergy has been shown by both clinical and laboratory tests to develop definite recurrent locations in circumscribed areas of the skin as well as of the mucocutaneous and mucous surfaces

In one of the cases reported the ulcerous lesion could be definitely traced to electrogalvanic currents produced by artificial dentures. In another, the gingivitis was definitely determined to be due to the mechanical phases of an ill-fitting denture.

Another patient was sensitive to the preparation used in the denture. The diagnosis of allergic oral disturbances is made by the recurrence of the lesions on the use of or contact with these agents and their disappearance after their elimination, the subjective symptoms being burning, tingling and actual pain

Food allergy was the most common finding, the most common causative foods in this series being chocolate, tomato, orange, egg, potato and milk. The ingestion of certain medicaments such as phenolphthalein, iodides, bromides and luminals may produce lesions of the mouth

Under differential diagnosis, the important lesions to rule out are the electrogalvanic phenomena, erythema multiforme, leukoplakia, thrush, lichen planus, secondary syphilis, pemphigus, herpes simplex, lupus erythematosus and the blood dyscrasias

Therapeutic Use of Thermal Agents

Sanford M Moose⁴ has discussed the highly controversial subject of the Rational Therapeutic use of Thermal agents with special reference to heat and cold, following operations in the oral cavity. In considering this subject, due cognizance was given the clinical opinion of many men engaged in the practice of oral surgery and exodontia as well as prominent members of the medical profession closely associated with dentistry. The questions asked were. Does the extra-oral application of heat or cold in phlegmonous tissue of the jaws have

any appreciable influence on the incubation of bacteria? What physiologic theory would you advance if asked why you prescribe ice compresses and why you prescribe hot compresses? What is the relative influence of hot or cold compresses on postoperative hemorrhage? Is the immediate postoperative or postextraction application of hot or cold compresses a predisposing factor in acute suppurative cellulitis or a subsequent osteomyelitis? In an analysis of the various opinions regarding and methods of application of the two thermal agents, heat and cold, as used in the practice of oral surgery the preponderance of evidence seems to favor heat as a physiologic agent

The application of cold is limited to early inflammatory stages, as an im-

pediment to the effects of trauma or up to the point of clinical evidence of exudation, beyond which process a decrease in temperature has a deleterious effect. The use of hot or cold applications in an effort to inhibit or destroy bacterial growth is so far beyond the safe physiological limits for tissue, that it can barely be considered. The use of heat, when potential infection exists, is the overbalancing belief in order to maintain, and promote inflammatory processes.

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SURGERY

Edited by Eldridge L. Eliason, AB, MD

ABDOMINAL SURGERY

By James Norman Coombs, M D

Attention has frequently been called to the advantage of early treatment of abdominal injuries. When dealing with penetrating wounds of the abdomen, the mortality and morbidity are in direct proportion to the interval between injury and active treatment. When death occurs within 24 hours after a penetrating wound, it is usually due to hemorrhage and shock, whereas when it occurs later, it is usually due to generalized peritonitis

Wounds of Abdomen

There has been a great deal of discussion as to whether operation should always be performed in wounds of the abdomen even when it is not certain that there has been penetration Mauro¹ discusses the question on the basis of 607 cases treated in the last decade at the Pelligrini Hospital in Naples 53 of which were his own Histories of 32 of the cases with descriptions of the operations are given. He gives a diagrammatic outline of the diaphragm showing the segments that are most frequently wounded, and another showing the organs wounded in his cases and the percentage of mortality tor each type of wound

In his war experience he succeeded in saving 66 66 per cent of his patients with severe lesions of the organs, this was better than the results which he obtained in the civil hospital where he succeeded in saving only 50 per cent

Among the 607 cases considered in this article 344 were operated with a

mortality of 31 97 per cent; 263 were not operated on, and presented a mortality of 19 08 per cent. In the non-operated cases operation was not performed either because the patient refused it, his condition was so hopeless that operation would have been useless, or 24 hours or more had passed since the injury, and the patient's condition was such that it seemed probable he would recover without operation

He discusses lesions of different parts of the colon and says that he believes that many patients with these conditions are lost because the part of the colon not covered with peritoneum is not inspected. In his cases this inspection made it possible to cure lesions that would otherwise not have been suspected. The soiling of the retroperitoneal tissue with intestinal contents is particularly serious.

In cases in which penetration was doubtful he inspected the external wound under local anesthesia, if penetration was not found he simply cleansed the wound and sutured it. If penetration was found he made an incision large enough to inspect freely the organ or organs probably wounded. He operated as rapidly as possible and avoided rough manipulations, especially of the mesenterium, to avoid any greater tall of blood pressure. He explored, as gently as possible, the retroperitoneal space in order to find lesions that are often overlooked. He removed tissues that were probably infected and provided for thor372 SURGERY

ough hemostasis and peritonealized the wounds with free or pedunculated flaps of omentum. He used meticulous care in cleansing the peritoneal cavity cases of recent wounds without soiling with intestinal contents he closed the wounds after giving electrargol or antiperitonitis serum In other cases he drained more or less freely with strips of gauze or a Mikulicz drain Meticulous postoperative care is the secret of success in many abdominal operations Glucose and saline rectoclysis, antiperitonitic serum, antipyogenic serum in cases which are probably badly infected, stimulants to intestinal movement when necessary, and particularly intravenous injections of hypertonic salt solution, Fowler's position, and tonics are recommended

Disruption of Abdominal Wounds

To establish correct figures for the incidence of evisceration and for certain factors that may affect it, F Glenn and N Moore2 made a study of the incisions in 2927 abdominal operations Twenty-two cases of evisceration were disclosed—an incidence of 0.75 per cent Catgut was used in closing 1608 wounds, silk sutures in 1144, and silver wire in 175 cases Mid left rectus and transverse rectus incisions are rightfully used with great reserve, for the incidence of evisceration in both is high. Of the usual incisions in the upper part of the abdomen, the upper left rectus carries the highest percentage of disruptions in this series Only one McBurney wound disrupted, in this case the closure was inadequate and the drains were of such bulk as to prevent the wound from closing Malignant conditions seriously affect the incidence and results of evisceration There were six eviscerations in patient operated on for malignant disease, they comprised 27 per cent of

the total eviscerations In 582 laparotomies for malignant manifestations there were six eviscerations, but in 2345 operations for nonmalignant diseases there were 16 eviscerations

Of the 16 eviscerations in the nonmalignant cases, six followed cholecvstectomies, the ten other eviscerations were associated with operations for peptic ulcer, postoperative hernia, ulcerative colitis, diverticulosis of the colon. bleeding from the gastrointestinal tract. appendicitis with peritonitis and pancreatitis Debility has been recognized as a possible cause of evisceration It was present in 11 of the 22 cases In no instance was jaundice or diabetes associated with the evisceration, although these conditions have been encountered frequently in surgical cases Evisceration occurred 13 times in incisions of the upper right rectus, twice in the upper left rectus, once in a transverse rectus, once in a mid left rectus, once in a McBurney, twice in lower left rectus and twice in lower right rectus incisions The single transverse rectus incision disrupted seven days after operation Of the 22 eviscerations 11 were wounds closed with catgut, seven with silk, three with through and through silver wire and one with through and through silkworm gut Disruption occurred from 1 to 16 days after operation, the majority on the fifth to the eleventh day after operation Secondary closures were effected in 18 of the 22 cases with through and through silver wire sutures None of these reopened In two cases the wounds were packed and strapped with adhesive tape and in two the wounds were resutured Following secondary closure, the patients remained in the hospital from 19 to 26 days The immediate mortality in this group of cases was 45 45 per cent (ten cases) A follow-up of the discharged patients showed that one died eight months later of cirrhosis of the liver and another, 22 days later, as the result of cancer.

A M Shipley³ reports two cases of wound disruption following a right rectus incision. In neither case was there any evidence of infection of the peritoneal cavity or of the incision. In both instances cholecystectomy was performed

but with the advent of better catgut he began to utilize the latter. He believes that there is no difference in the two suture materials from the standpoint of wound disruption

He divides wound disruption into cases with infection and clean cases. It is in the latter group that considerable anxiety is caused

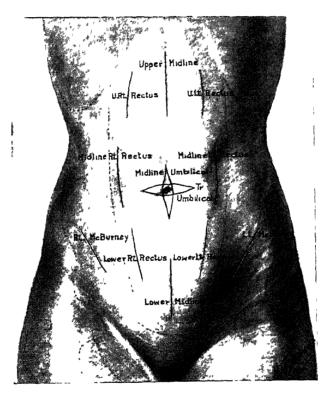


Fig 1—Location and designation of incisions employed (Drs Frank Glenn and S W Moore The Disruption of Abdominal Wounds—A report on 22 Cases, in Surgery, Gynecology and Obstetrics July, 1937)

Careful examination of the wound edges from the skin to the peritoneum failed to reveal any catgut except two knots which were lying free, and these were in the late stages of disintegration

The writer emphasizes the importance of wound disruption, and reviews a number of papers that appeared on the subject in the last few years

He states that in the early years of his experience he used the silk technic, The author concludes with the hope that very careful attention to the subject will solve the problem

Catgut Allergy and Wound Disruption

Intrinsic factors altering the absorption of catgut is discussed by C J Kraissl ⁴ The author states that the presence of flaws and foreign bodies in catgut emphasizes the necessity for careful

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examination of the product before it is used Some method of supply other than in narrow glass tubes which kinks the gut at each bend should be devised

By making catgut anhydrous so that it may be boiled, its properties of flexiIt is possible to sensitize guinea pigs to catgut and to produce disruptions of laparotomies sutured with this material Non-allergic patients may be occasionally sensitive to it while allergic patients are quite often sensitive. The highest



lig 2-4 Bent strands are noticeable B and C, Foreign bodies in catgut D, Flaw in catgut leaving only about half the normal width of the strand (Dr Cornelius J Kraissl Intrinsic Factors Altering the Absorption of Catgut in Surgery, Gynecology and Obstetrics, Nov., 1936)

bility are lost and in most cases its absorption time is shortened

During absorption of the protein in catgut, the metals and halogens it contains are liberated and may set up a local irritation in the tissue, thus interfering with wound healing. This is particularly true of chromium to which individuals may also be sensitive.

which wound disruption had occurred and all allergic patients who had disrupted exhibited a sensitivity to one or more antigens. There may be a relationship between wound disruption and sensitivity to catgut or chromic acid in certain individuals, particularly if they have a history of allergy, previous operations,

or exposure to chromic acid. It is recommended that if catgut is to be used, particularly in these instances, the sensitivity of the individual should be determined by appropriate skin tests.

Postoperative Wound Infections and the Use of Silk

Clinical experience has shown P Shambaugh and J E Dunphy⁵ that in clean wounds postoperative infection occurs less frequently where fine silk has been employed as suture material than

trol the factors which attended the initial contamination

As the fear of the consequences of infection still constitutes the chief obstacle to a more general adoption of the silk technic, it seemed desirable to study more carefully the comparative healing of contaminated silk and catgut wounds. The authors have, therefore, investigated this problem in the experimental laboratory and have been able to demonstrate by controlled observations the superior resistance of silk wounds to infection

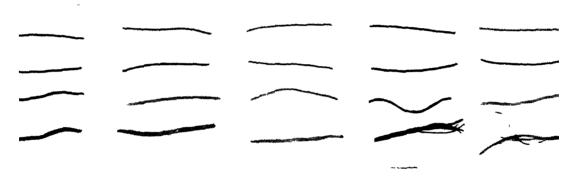


Fig 24—Changes in strand and texture after immersion in dilute base (Dr Cornelius J Kraissl Intrinsic Factors Altering the Absorption of Catgut, in Surgery, Gynecology and Obstetrics, Nov., 1936)

where catgut has been used This difference may be attributed to the fact that silk is much less irritating to the tissues and does not itself provide a favorable medium for the growth of bacteria. The silk wound is thus better able to tolerate a slight bacterial contamination which might in the catgut wound result in suppuration. The observations and statistics which have led to these conclusions are, however, open to the just criticism that they are necessarily compiled from more or less uncontrolled data Obviously, we cannot in the clinic deliberately contaminate wounds to observe their resistance to infection, and where suppuration unfortunately follows a clean operation, it is impossible to conThe authors have, likewise, been able to confirm an observation previously made in the clinic, which is contrary to accepted opinion, namely, that suppurating silk wounds may in certain instances completely heal without the removal or the spontaneous discharge of the fine silk sutures and ligatures

The comparative healing of heavily infected silk and catgut wounds was studied in ten experiments. Gross suppuration occurred in the catgut wound in every instance, whereas, the silk wound in four experiments healed without suppuration (Fig. 2B). In four experiments, the silk wound suppurated, but the wounds showed considerably less reaction than the corresponding catgut

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wounds, and the suppuration occurred at a later date. In the remaining two experiments, both the silk and the catgut wounds showed about the same reaction and both suppurated at about the same time.

The authors were particularly interested in following the healing of the silk wounds in which suppuration oc-

sinus persisted for seven months, at which time the animal was sacrificed and dissection of the wound showed a long suture lying at the bottom of the sinus. The fine interrupted silk sutures, however, were all in place and were not in communication with the sinus

There were eight silk wounds in which suppuration occurred All of these, with

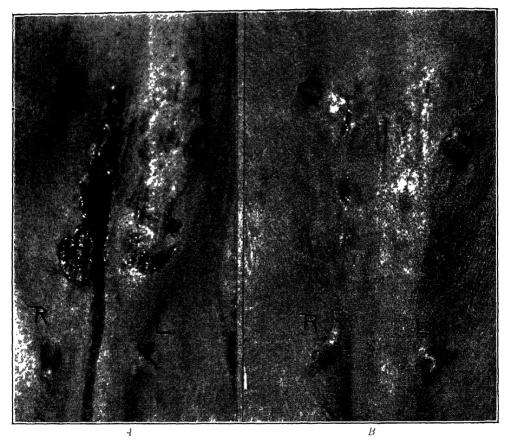


Fig. 2B—Photograph showing the comparative healing of infected wounds which have been sutured with catgut on the right side (left side in photograph) and with silk on the left side 1 on the tourth postoperative day B, on the twenty-first postoperative day. The catgut wound broke widely open and discharged a thick purulent exidate. The silk wound, although it became red and swollen did not suppurate. Post-mortem dissection, three months later, showed the silk sutures in place without gross evidence of infection. (Courtesy, Surgery, March, 1937.)

curred. All except one of them healed as quickly as the corresponding catgut wound, the average period of healing being 25 days. The single exception was one of the two instances in which a continuous silk suture was used to close the peritoneum. In this case, a small

the exception of the above instances, healed firmly within 28 days and remained healed as long as observed for intervals up to 12 months. Seven of the wounds were dissected postmortem. The silk sutures and ligatures were found in place with little or occasionally with no

gross tissue reaction. Those in the muscle showed no reaction, whereas, the bits of black silk in the fascia and subcutaneous tissues were frequently found to lie in a tiny area of fibrosis or of

Histologic studies of the silk wounds, which were heavily infected, gave definite evidence that satisfactory healing had occurred without discharge of the silk sutures (Figs 2C and 3)

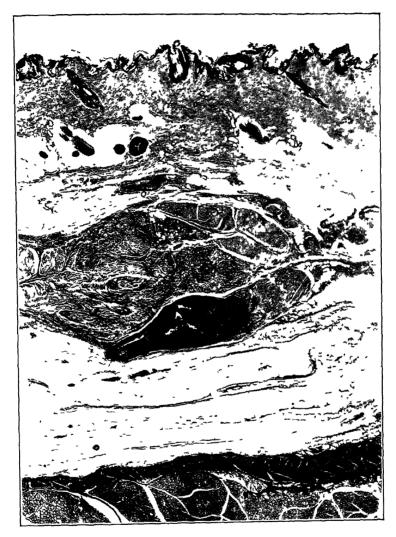


Fig 2C—Photomicrograph of a heavily infected wound which was closed in layers with fine silk sutures four months after operation. Gross suppuration occurred but healing was not delayed by discharge of sutures, and there were no persistent sinuses. Note the well-encapsulated black silk suture (4) and the almost invisible scarring of the line of incision (×12). (Courtest Surgert March, 1937.)

yellowish jellylike material In no case, however, was an abscess found In one experiment, aerobic and anaerobic dextrose broth cultures were made from the tissues about the silk sutures 12 months postoperatively. No growth was obtained

In one of the experiments, the postmortem dissection disclosed an interesting finding Both the silk and the catgut wounds had suppurated and healed Seven weeks later the animal was sacrificed. The silk wound showed all the sutures in place with a small amount of 378 SURGERY

the jellylike material about several of them, but no fluid or purulent material The catgut wound, however, contained three indurated areas five millimeters in dence in the tissues Apparently catgut may occasionally, even in the presence of infection, resist absorption and remain unchanged in the tissues for a consider-



Fig. 3—Higher magnification of the encapsulated silk suture shown in Fig. 2C. Although there are still polymorphonuclear leukocytes present, the strands of silk are surrounded by fibroblasts and mononuclear cells (\times 900) (Courtesy, Surgery, March, 1937)

diameter lying in the subcutaneous layer, each containing a small firm catgut knot lying in cloudy fluid. The catgut did not appear altered by its two months' resi-

able period This concurs with clinical experience, the authors having observed instances of complete healing being delayed by bits of unabsorbed catgut

Keloids Following Laparotomy

According to J C Wood,⁶ wound infections, cicatrices of all forms, and postoperative hermas are much less frequent now than formerly—thanks to the evolution of a more ideal technic But keloids, it seems to the writer, still occur all too often Because of the fact that, when present in an abdominal scar, they are less conspicuous than when present in exposed areas, their importance has been underestimated

The following procedures are used by Wood

General or spinal anesthesia is used. Local anesthesia, especially when used in excess, has a tendency to devitalize the tissues

Careful asepsis is never, no matter how rigidly observed, 100 per cent perfect, therefore, the skin incision is made with scalpel number one Scalpel number two is used to divide the underlying structures. All active bleeding is controlled but moderate oozing is ignored

The operation completed, the peritoneum is brought together with a fine, plain gut suture

Three to five silkworm tension sutures are introduced from within outward, the same needle never being used twice during the operation Exit of the needles is at least two centimeters from the wound edges. The sutures should include, other than the layers of fascia and the recti, the ridge of tissue resulting from the closure of the peritoneum, so that, when they are finally tied, there will be no dead space between the peritoneum and the intervening fascia. These sutures are left untied until the skin clamps are applied.

The deep fascia, either edge to edge or overlapping, is carefully sutured with chromic gut No 1 or 2, as few knots as possible being left

The skin wound is closed with Michel clamps, so placed as to make it possible to remove them with minimum trauma to the healing skin wound behind. Before the last one or two clamps are applied, pressure is made from below upward with a gauze sponge for the purpose of expressing any accumulated blood or serum from the wound.

The interrupted sutures are tied over narrow strips of gauze, saturated in 95 per cent alcohol, placed on either side of the clamps, just tightly enough to control all oozing. Unless the clamps are thus protected, unnecessary suffering ensues, both from the tension sutures and from direct pressure upon the clamps, when the outer dressings and binder are applied. The alcohol serves a most useful purpose as a destroyer of germs.

The tension sutures are removed not earlier than the fourth day and the clamps not earlier than the fifth day following the operation After their removal, the skin wound is sustained for at least three weeks by the application of butterfly adhesives, the wound being protected by an underlying strip of sterile gauze Adhesive plaster should never come in direct contact with the skin wound, even though its center is smeared with an antiseptic, for at least ten days following the operation It cannot be made absolutely sterile and, when so placed, frequently results in slight skin infection, which is often the forerunner of a keloid

This summary is deduced not, as Wood has emphasized, from accurate statistical data, which would be quite impossible to obtain from the case records of any consulting surgeon whose clientele is scattered far and wide, but rather from such cases as have subsequently returned to the author for reexamination, or for newly developed

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symptoms During the last 15 years, the author's hospital has especially stressed for their internes the closing sentences of the previous paragraph with correspondingly better results

Profusely Draining Abdominal Wounds—A method of dealing with profusely draining abdominal wounds has been described by J B Lounsbury 7 In the treatment of abdominal wounds having abundant discharge as well as being chronically infected, two major problems arise. The first is that of the dis-

materials required are sufficient rubber tubing, glass connectors, Montgomery adhesive straps, a de Pezzer catheter, rubber band, vaseline, and a "Daisy" suction cup No 400 The latter is an adaptation of a sucker used to clean sink drains, better known as "the plumber's friend" (Fig 4) It can be obtained at any department store

From the rubber cup of the "plumber's friend," that portion is cut into which the handle fits A hole 1 cm in diameter is cut in the top for an air inlet

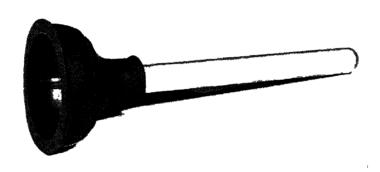


Fig. 4— The plumber's triend. The handle is removed and the rubber part into which it fits is cut off flush with the top of the cup. (Courtesy, Annals of Surgery, Sept., 1937.)

posal of excessive secretions and excretions which seem to evade the bounds of dressings, even though the latter be frequently changed. In addition to the discomfort of the patient in lying in a constantly unclean bed, the application of several dressings daily is a needlessly time consuming task and unnecessary expense. The second problem to be faced is that of applying the fundamental surgical principle of keeping a wound clean in order that healing may progress.

In an effort to find the solution of these two problems in the routine care of such patients, the simple suction apparatus presented herewith has been devised

The primary requisite is the availability of *continuous suction* The

About 1 cm above the rim of the cup another hole is made of sufficient size so that a No 30 or 32 F de Pezzer catheter will fit snugly The rubber cup used is rigid enough to retain its shape, and yet plastic enough to conform to the contours of the patient's body The brim of the cup is sufficiently wide to prevent its cutting into the skin of the abdomen with the pressure exerted The air inlet prevents the development of a partial vacuum which might severely traumatize the tissue By the use of a de Pezzer catheter and the arrangement of it so that one hole in its tip will be next to the wound and the other toward the top of the cup, a free passage way is assured in the event that tissue should be sucked into the lower opening The arrangement

of this portion of the apparatus is shown in cross-section in Fig 5

In setting up the apparatus in its simplest use, the skin of the abdomen is relatively thickly covered with vaseline from the margins of the wound outward to a distance comparable to the diameter of the cup. This not only makes a watertight contact of the cup with the skin, but serves to protect the skin from irritating secretions or excretions. The cup is placed over the wound and secured in place by two Montgomery straps joined.

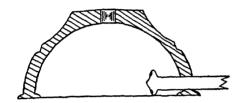


Fig 5—Cross-section of suction cup with the de Pezzer catheter in place (Courtesy, Annals of Surgery, Sept , 1937)

by a rubber band A great amount of tension of the rubber band is not necessary, and indeed is undesirable, since too much pressure upon the skin may produce edema of the area within the cup The catheter is connected to the suction and the apparatus is ready for use Figs 6 and 7 illustrate this set-up in use. The patient shown had far advanced urmary tract tuberculosis with stricture of the urethra The cystostomy wound gradually broke down around the drainage tube so that a water-tight wound could no longer be maintained, and urine leaked from around the tube to such an extent that the patient and his bed were almost constantly wet Since the application of the suction cup the reverse has been the case, and, whereas three or four changes of bedclothing daily were previously necessary, now the routine morning nursing care suffices for the remainder of the day

A secondary appliance for this apparatus is the introduction of an irrigating mechanism. This can be effected by making another small hole in the top of the suction cup, through which a soft rubber catheter is introduced leading through the cystostomy wound into the

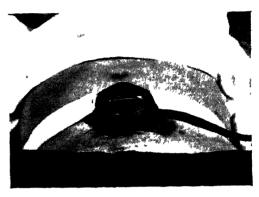


Fig 6—Front view of the simplest arrangement of the suction cup, showing the Montgomery adhesive straps and rubber band in place

(Courtesy, Annals of Surgery, Sept, 1937)



Fig 7—Same as Fig 6, side view (Courtesy, Annals of Surgery, Sept., 1937)

bladder To this catheter is connected a reservoir of irrigating solution. Fig. 8 shows this outfit in operation in a patient with a necrotic and secondarily infected cystostomy wound. As stated intervals about 100 cc. of solution are

allowed to run into the bladder and well up through the cystostomy wound to be sucked off from the confines of the cup

A further arrangement for irrigation of a chronically infected cystostomy wound is demonstrated in Fig 9 with the addition of the bladder irrigating apparatus adapted from the Connell apparatus. The indwelling urethral catheter serves for the introduction of the irrigat-

be incorporated into the simplest suction mechanism (Figs 6 and 7) by a glass Y-tube While the suction is momentarily pinched off, about 50 cc of solution are allowed to run into the suction cup loosening the feces and lavaging the fistulous opening. The tube from the reservoir is then closed and the suction opened to remove the solution and suspended fecal material



lig 8—Suction cup with one method of irrigation shown. The catheter, entering the top of the cup and connected with the reservoir, extends into the bladder. The larger de Pezzer catheter seen in the foreground connects to suction. (Courtesy Annals of Surgery, Sept., 1937.)

ing solution, about 150 cc at intervals, which passes upward through the wound into the cup from which it is sucked away. In the meantime between irrigations, urmary drainage is effected in the usual manner through the urethral catheter into a container beneath the bed

Another adaptation of this method is suggested in the care of fecal fistulae A reservoir of irrigating solution may

The use of the suction apparatus and its adaptations described above has been but recently instituted in a few cases, but its effectiveness in disposing of excessive secretions from cystostomy wounds, and in permitting a method of irrigation, has in this short time proved so successful as to be worthy of attention. Its simplicity of construction is also to be recommended.

Auscultation in Acute Surgical Conditions of the Abdomen

For several years A Charbonnier⁸ has been making a systematic examination with the stethoscope of all patients whether treated surgically or otherwise. After accumulating a great many observations he reports his conclusions regarding the value of this procedure His article includes a bibliography referring

cultation of the lungs and heart. It is a method that can be used at the bedside without inconvenience to the patient. Skill in the use of the stethoscope in abdominal diagnosis is easy to acquire. However, a thorough knowledge of the normal sounds in the abdomen is essential to distinguish sounds that are abnormal and to draw accurate conclusions as to their causation. The surgeon must

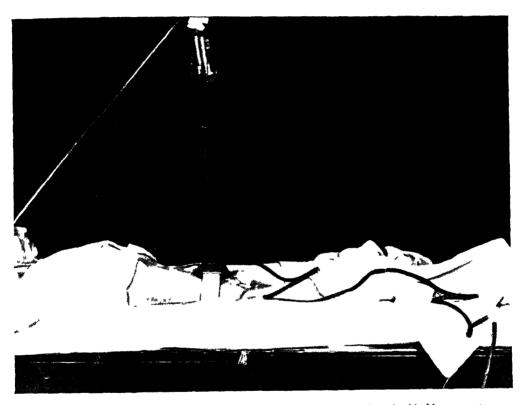


Fig 9—Suction cup showing urethral catheter in place connected to the bladder irrigating apparatus adapted from the Connell arrangement (Courtesy, Annals of Surgery, Sept. 1937)

chiefly to the French and Italian literature and résumés of a large number of case histories

He points out that as auscultation of the abdomen has been practiced so imperfectly and so irregularly up to the present time judgment of its value has been heretofore impossible. After his wide experience he believes that such auscultation is just as important as ausbe able to recognize modifications of the normal peristaltic rhythm (hyperperistalsis) and hypoperistalsis), to distinguish the difference in rhythm and in timber of the sounds characteristic of the stomach, the small intestine, and the colon, and, in addition, to interpret the variations in tone and resonance produced by gaseous or hydrogaseous distention of the intestines

Auscultation is of particular value in confirming the diagnosis of peritoritis, volvulus, and perforation In cases of abdominal distention it may aid in the localization of an obstruction by making it possible to distinguish a solid from a cystic tumor or by revealing intraperitoneal reactions. Charbonnier emphasizes that under all of these circumstances it should be used only as a supplement to other diagnostic methods. For success it must be done systematically and sufficiently long at a time, and must be frequently repeated.

The sounds heard in the abdomen are divided into passive and active sounds. Among the former are peritoneal rubs due to the movement of the abdominal wall and the diaphragm in respiration. Under certain conditions other passive sounds may be produced by cardiac or aortic pulsation, but these are very rare

The active sounds are produced by the automatic movements of the abdominal viscera. The most important is what Charbonnier calls the "peristaltic murmur". After reviewing the normal physiology of all portions of the intestinal tract. Charbonnier describes the variations of this normal sound. Free fluid produces a double bruit in quick succession like the sensation obtained on percussion. Encysted fluid transmits the peristaltic murmur and has a metallic resonance to light tapping.

Charbonnier urges that the following procedures be carried out in the cases of all patients

- 1 Auscultation of the peristaltic murmur Rhythm, exaggeration, diminution, or absence of the murmur, and the murmur produced in the small intestine, colon, stomach, and pylorus should be noted
- 2 Auscultation to determine the tone and quality of the murmur and other

sounds The variation depends upon the degree of abdominal distention

3 Auscultation for (a) Passive sounds, e g, peritoneal rubs and rubs produced by pressure of the hand, (b) intra-abdominal adventitious sounds such as those produced by the escape of liquid through a perforation and by vascular thrills, and (c) extra-abdominal sounds such as osseus crepitation and pleuro-pulmonary sounds

Charbonnier describes the changes in the various murmurs described and the adventitious sounds that may be expected in the following surgical conditions of the abdomen (1) Intestinal obstruction and volvulus, (2) acute generalized and localized peritonitis, (3) accidental and spontaneous perforation of the intestinal tract, (4) inflammation of intraperitoneal and retroperitoneal viscera, (5) ilomesenteric infarction, and acute dilatation of the stomach

Abdominal Incisions

F S Lynn and H C Hull⁹ believe that in selected cases of definite pathological conditions in the upper abdomen the transverse abdominal incision is ideal as it gives most satisfactory exposure and permits easy and secure closure They state that the object of any abdominal incision is threefold (1) Adequate exposure, (2) secure and reliable closure, and (3) the prevention of hernia They believe that the transverse incision meets all of these requirements better than incisions of other types They contend that usually a vertical incision is converted into a transverse incision by lateral retraction, and that sometimes the force is so great that the structures of the abdominal wall are traumatized

Attention is called to the fact that the transverse abdominal incision is an old one, it having been used first in 1847 by Baudelocque for caesarean section

Anatomically, the incision is very good for the following reasons:

- 1 The cleavage of the skin is transverse to the long axis of the body.
- 2 The rectus sheath above the semilunar fold of Douglas is formed by aponeurosis of the external oblique and anterior and posterior lamellae of the internal oblique. The fibers of all of these structures course in a transverse direction
- 3 The tendinous insertions run transversely to the recti muscles situated at the umbilicus, the lower border of the xiphoid, and midway between. The seventh, eight and ninth intercostal nerves run just below these landmarks. It is desirable to avoid cutting these structures because they act as a strong splint to the recti muscles. The main intercostal nerve and even its minute branches course in a transverse direction in the operative site. Therefore the incision does not sever any important nerves.
- 4 Because of the extensive anastomoses, severance of vessels by the transverse incision, which runs at right angles to them, is not unfavorable

In coughing, sneezing, and straining, the edges of the wound made by a vertical incision tend to be pulled apart, whereas those of the wound made by a transverse incision tend to be approximated

Sloan reports that there is 30 times more pull in a vertical closure than in a transverse closure. After operations performed with a vertical incision, inhibition of thoracic movement to splint the incision and thereby relieve pain favors atelectasis and pulmonary hypostasis.

The transverse incision is made through all of the structures from the abdominal wall to, and including, the peritoneum. The tendency toward evisceration is less in such an incision than in vertical incisions. In the closure of

the transverse incision it is often helpful to "jackknife" the table. The wound is closed in the usual manner, the peritoneum and posterior aponeurosis being sutured in one layer

The transverse incision is of advantage to the patient because it reduces the amount of anesthetic and gauze packing required and is followed by less wound reaction, shock, and pain and by fewer postoperative complications It is of advantage to the surgeon because it is more anatomically correct than other incisions, it is physiologically correct, it gives excellent exposure and therefore reduces handling of the viscera to the minimum, the use of retractors is usually unnecessary, it permits easy, secure, and reliable closure; it is less apt than other incisions to be followed by fascial slough or hernia: it is followed by less pain than other incisions; it yields better end-results in the presence of infection, and it is ideal in selected cases of definite disease

Its disadvantages are that it cuts across the recti muscles, bleeding is a little more profuse than when other incisions are used; and it is not an ideal incision for all abdominal viscera

Operation for Relief of Pain in Incurable Abdominal Diseases

A new operation which suppresses abdominal pain by resecting the lumbar sympathetic and splanchnic nerves is described by J Diez 10 The operation is done under local anesthesia by infiltration of a five per cent solution of procaine hydrochloride. The patient lies in the lateral position with flexed legs and a pillow under the side opposite to that on which operation is performed. A 2 cm incision is made from the twelfth rib and the muscles of the vertebral canals to a point above and behind the anterosuperior iliac spine. The operation consists in retroperitoneal approach and

resection of 2 or 3 cm of the major and minor splanchnic nerves and of the lumbar sympathetic The latter is resected from the point at which it issues from the diaphragm to the third lumbar ramus communicans. As a rule the operation is bloodless. The operative wound is closed in four planes without drainage. The operation must be bilateral, otherwise pain recurs The second operation is done ten days later by the same technic The sensitivity of all the abdominal viscera, except that of the pelvic ones, as well as that of the anterolateral parietal peritoneum, is suppressed The operation is indicated in incurable abdominal diseases, especially cancer, which lack a causal treatment. It can be done even in cachectic patients. The general and nutritional condition of the patients does not improve, but their sufferings are greatly relieved without danger from the treatment.

APPENDICITIS

The Appendix Problem — There were 18,129 deaths from appendicitis in the United States during 1934, while the deaths between 1900 and 1934 have never mounted higher than 153 per 100,000 population

E P Hogan¹¹ points out that appendicitis is a neglected medical educational problem. The subject of appendicitis does not εven appear in many recent authoritative treatises on gastroenterology and the practice of medicine.

Hogan traces the surgeon's experience with appendicitis from the time appendicitis was recognized as an entity, and recounts the varying trends of opinions concerning its treatment. As more experience has been gained, the mortality has decreased. Hogan urges now that the public be educated regarding this condition as he believes that thereby further

reduction of the mortality rate can be accomplished It is well established that early diagnosis is the keynote of treatment, and the patient's knowledge of the disease will do much to make a clinic history more accurate.

The type of treatment employed has a definite bearing upon the mortality Various surgeons have somewhat different views on the subject of treatment, and he reviews the opinions of many outstanding surgeons, and refers to the large series of cases reported by them He believes that the intensive study being made of appendicitis accounts for the reduction of the mortality as shown by the records of official statisticians More than 90 per cent of the mortality reported is due to some form of peritonitis

The author then concludes with the statement that a broad educational campaign, national in scope, will decrease the number of cases of appendicitis which come under observation after inflammation has extended beyond the appendix

Pathology-Seventy gangrenous appendices obtained by operation were examined bacteriologically and histologically by Shiro Suzuki 12 At the same time 17 normal appendices, as well as appendices obtained in early or interval operations, were examined as controls The contents were examined bacteriologically, and sections were examined bacterioscopically by means of Gram's coloring matter and the silver impregnation method of Levaditi In all gangrenous appendices, edema, hemorrhage, cell infiltration and tissue necrosis were found to be more or less pronounced, and occasionally severe necrosis of the lumen with perforation was observed The gangrenous process was least pronounced at the base of the appendix and most pronounced at the tip Bacteriologically the contents of the appendix yielded many typical and atypical colon bacilli; and in individual cases, enterococci, pyocyaneus bacıllı, staphylococcı, and ın one case a type of anaerobe were found in culture Colon bacılli, enterococci, or proteus bacıllı, as well as anaerobic organisms were observed generally also. Bacterioscopically many different types of bacteria were obtained from the necrotic layer of mucosa and submucosa lying near the lumen There were long and short rods with Gram-positive coloring, and a few Gram-positive monococci, streptococci-like cocci, Gram-positive diplococci, and other micro-organisms In the deeper structures of the appendix wall the variety and number of bacteria decreases In the muscularis and subserosa only a few Gram-positive diplococci and monococci and short rods were found In the non-gangrenous appendices only monococci and diplococci were observed The bacterioscopic findings were not always parallel with the degree ct histological changes Only in extensive necrosis many different bacteria entered the deeper structures From the findings in early gangrenous as well as phlegmonous appendicitis it was observed that ulcerative processes, epithelial defects, or necrosis must be present in order that the bacteria in the lumen can enter into the deeper tissues

To determine the mechanism and significance of obliteration of the lumen and vermiform appendix, 1054 appendices obtained in consecutive autopsies at the Mayo Clinic and 300 removed surgically at St Mary's Hospital, Rochester, Minnesota, were studied *in situ* by D C Collins¹³ and examined grossly and microscopically after removal The sections for microscopic study were made at the tip, the center, and the base

Of the gross diagnoses as to the presence or absence of lumen obliteration, only 39 per cent were incorrect. In the great majority of instances the error

was due to failure to recognize very early degrees of obliteration. The incidence of obliteration was greater in retrocecal appendices than in appendices lying in an anterior position, and greater in shorter appendices than in appendices longer than 6 cm.

It was only in the cases of subjects above the age of 40 years that total lumen obliteration was found to any appreciable degree. Only 22 per cent of all lumen stenoses occurred before the age of 40, while 80 per cent occurred between the ages of 30 and 70 However, the fact that 50 per cent of the specimens in each age group before the seventh decade were still patent seems to the author to demonstrate that involutionary processes cannot entirely explain the mechanism of lumen obliteration.

Five carcinoid tumors were found Accordingly, there was one carcinoid tumor to every 82 cases of obliteration All of these neoplasms were found in obliterated portions of the lumen.

Two types of inflammatory obliterative processes were differentiated author describes the histologic characteristics of each in detail. He states that the type of reticulum and collagen encountered in an obliterated appendiceal lumen is comparable to that observed in granulation tissue and in scars healing by secondary intention elsewhere in the body He was able to find no proof that the sympathetic nerve plexuses of the appendiceal wall or neuromas formed from argentaffine cells play any appreciable rôle in the formation of new connective tissue present in the obliterated lumen He believes that the carcinoid tumors are derived as a rule from submucosal epithelioneurogenic elements

He cites the following factors as playing important rôles in the mechanism of obliteration of the appendiceal lumen:

1 The vestigial nature of the appendix.

2 The terminal type of its blood supply.

- 3 The involutional process that begins in the appendix as in all other body tissues at about the age of 25 years
- 4 Progressive obliteration of the capillary bed of the appendix after maturity is reached, similar to that occurring in the capillary beds of all parenchymatous organs
- 5 The well-known mability of the appendix to cope with even mild infection
- 6 The tendency of adipose tissue to collect in the appendiceal submucosa
- 7 Histological changes due to inflammation
- 8 The tendency of all organs containing an excess of lymphoid tissue to undergo involution after maturity

The author believes that the greater trequency of obliteration of the appendix in older individuals is more apparent than real as in older persons the condition is often due to an inflammation early in life

He concludes that obliteration of the appendiceal lumen occurs largely as the result of inflammation which destroys the mucosa and portions of the submucosa, involution being merely a contributing factor

The appendicular syndrome without an appendix is commented upon by R Caminiti 14. Up to the eighth week of fetal life there is only one cecal sac. Thereafter the upper part enlarges to form the cecum, while the lower part shows only a limited growth and forms the appendix. In some cases the latter development may be arrested and the child born without an appendix. The author came across one such case among 243 operations for appendicitis. The most exact and prolonged searching on the

operating table did not reveal any trace of an appendix. The cecum was found to have a perfectly normal shape, and only the adhesions around it accounted for the clinical picture which had led to the diagnosis of appendicitis. The patient was benefited by the solution of the adhesions

Medical literature, old and new, contains accounts of about 50 such cases. which were found either on the operating table or at autopsy The author discusses the possibility of destruction of the appendix by pathological processes or by senile involution Even after making an allowance for such destruction, there always remain cases of complete agenesia of the appendix and cases in which there is at least a small button as a hypoplastic substitute However. these anomalies are so exceedingly rare that the knowledge of their existence should never detain a surgeon from undertaking an intervention if it seems to be indicated

Hemography in the Diagnosis of Appendicitis—W J Crocker and E H Valentine¹⁵ state that they have modified the Schilling classification of neutrophils, and on the basis of a study of 500 cases of appendicitis treated at the Philadelphia General Hospital believe they can differentiate eight degrees of appendicitis from the hemogram

They describe the normal hemogram as consisting of 0 myelocytes, 0 juveniles, four stabs, 64 segmenters, a normal Schilling index of $\frac{1}{16}$ or a multiple index of one

They believe that much valuable information is obtained from a comparison of the number of neutrophil types, since a left shift with greater numbers of myelocytes and juveniles is indicative of a more serious state than a left shift consisting largely of stabs

The eight degrees of appendicitis they distinguish and the corresponding hemograms are as follows:

First degree or chronic fibrous appendicutes White cell count, from 5000 to 10,000, neutrophils, from 40 to 70; total shift cells, from 10 to 35, Schilling index, from ¼ to 1, and a left shift limited almost exclusively to stabs

Second degree appendicitis, including those conditions commonly classified as chronic inflammations of the appendix Instead of inflammation, however, there may be degeneration, atrophy, or hypertrophy With vague symptoms and a history of recurrent attacks the hemogram is rather constant white cell count, from 10,000 to 15,000, neutrophils, from 50 to 75, total shift cells, from 15 to 35, Schilling index, from ½ to 1, and multiple index, from 5 to 17

Third degree or acute suppurative carly gangrenous appendicutes. With typical symptoms of acute appendicutes the hemogram is constant white cells, from 15,000 to 30,000, neutrophils, from 75 to 95, total shift cells, from 15 to 35, Schilling index, from $\frac{1}{40}$ to $\frac{1}{10}$, multiple index, from 3 to 16, and lymphocytes, from 2 to 25

Fourth degree or acute suppurative exacerbation of a chronic appendicitis. With a history of recurrent appendicitis and a present acute attack the findings are constant, white count, from 7000 to 15,000, neutrophils, from 60 to 75, total shift cells, from 35 to 60, lympho cytes, from 20 to 40, Schilling index, from one to three and multiple index, from 16 to 48

Fifth degree or acute suppurative appendicitis with rupture and a mass in the right lower quadrant of the abdomen, walled off. In the presence of a history and symptoms of rupture of the appendix and a mass in the right lower quadrant of the abdomen the characteristic hemo-

gram is white count, from 10,000 to 30,000; neutrophils, from 60 to 90; total shift cells, from 35 to 60; lymphocytes, from 5 to 30; Schilling index from one to three, and multiple index from 16 to 48

Sixth degree or acute suppurative appendicitis without rupture. In the presence of a history of a first attack and acute symptoms the hemogram is as follows: white cell count, from 7000 to 30,000, neutrophils, from 75 to 95; total shift cells, from 35 to 60; lymphocytes, from 0 to 20, Schilling index from one to three, and multiple index, from 16 to 48

Seventh degree or acute suppurative appendicitis with rupture or impending rupture. In the presence of a history of a first attack and acute symptoms the hemogram is approximately as follows: white count from 6000 to 35,000, neutrophils, from 80 to 95, total shift cells, from 60 to 75, lymphocytes from 0 to 15, Schilling index, from 17 to 4; and multiple index, from 27 to 64

Eighth degree or acute suppurative appendicitis with rupture and diffuse peritonitis White cell count, from 5000 to 40,000, neutrophils, from 75 to 100, lymphocytes, from 5 to 25, Schilling index, from 4 to 100, and multiple index, from 64 to 1600

Representative shifts as shown by the tables are exemplified by the following

| Degrees | Myelo- cytes | Juve- niles | Stabs | Seg- menters |
|-------------|-----------------|----------------|----------------------|----------------------|
| 1 2 3 | 0 0 0 | 0 0 0 | 19 26 22 43 | 39 40 62 |
| 4 5 6 | 0 0 0 | 0 0 | 43 43 52 61 | 28 29 33 30 |
| 8 | 4 | 12 | 60 | 8 |

The significance of the obstructive factor in the genesis of appendicitis by ex-

periments on animals and by careful observation of the frequency with which obstructive phenomena are noted in the spontaneous occurrence of the disease in man has been evaluated by O H Wangensteen and W. F Bowers 16 In the dog complete obstruction of the infected cecal appendage was always followed by inflammation, obstruction of the washed appendage was usually well tolerated The essential inciting factor would appear to be a disturbance in the pressuredistention relationship of the appendix Sustained intraluminal pressures of from 8 to 15 cm. maintained for from 6 to 18 hours invariably were followed by changes in the wall of the cecal appendage. There appears to be a sphincterlike mechanism at the base of the appendix which makes of it a potential closed loop, with all its attendant inherent dangers This mechanism accounts for the formation of appendical stones or concretions. These are laminated and are formed largely in the appendix, a sign of appendical stasis Appendical concietions are found as acutely obstructing agents in most instances of perforated appendices-the group in which mortality occurs Appreciation of the significance of appendicular colic should lead to a better understanding of the nature of appendicitis Appendicular obstruction brooks no delay and demands immediate appendectomy

Diverticula of the Vermiform Appendix

D C Collins¹⁷ has reviewed the literature on diverticula of the appendix from 1918 to 1934. In examinations of 16,044 appendices removed at operation or autopsy, 67 diverticula were found. The average incidence of diverticula in the appendices covered by 11 reports was 0.42 per cent. Of 60 diverticula reported in the literature, 55 per cent.

occurred in the middle of the appendix, and 599 per cent were single Sixty-three per cent were on the meso-appendiceal border, and 36.7 per cent on the free portions of the wall

Collins has studied 30 appendiceal diverticula which were found in 23 (0.77 per cent) of 3017 appendices removed surgically and seven (0.66 per cent) of 1054 appendices examined at autopsy.

The diverticula were located at the tip and in the distal third of the appendix in 5977 per cent of the cases, in the middle third in 2929 per cent, and in the proximal third in 11.12 per cent.

In 43 29 per cent they were at the meso-appendiceal border, and in 56 61 per cent elsewhere on the free portion. In the author's opinion this fact indicates that the majority of appendiceal diverticula are of inflammatory origin

In 2997 per cent of the cases the diverticula were single. In 60 per cent they were associated with acute inflammation, and in 166 per cent had perforated. In three cases perforation of the diverticulum had resulted in pseudomyxoma peritonei.

The abnormal thickening of the walls of the appendices and the stenosis of the lumen which were invariably associated with the presence of a diverticulum are shown by illustrations. In the author's opinion, both of these changes are indications of an inflammatory origin of the diverticula. The stenosis is probably an important causative factor. Only two of the diverticula reviewed were believed to be of congenital origin.

In conclusion Collins states that appendiceal diverticula are of importance because acute inflammation of an appendix with a diverticulum produces atypical signs and symptoms and commonly early rupture which often results in generalized peritonitis of pseudomyxoma peritonei Therefore during the course of

abdominal exploration the appendix should be examined for diverticula, and if a diverticulum is found, appendectomy should be done.

Varieties of Appendicitis

Acute Pelvic Appendicitis - According to H. Brunn¹⁸ the most constant symptom of acute pelvic appendicitis is pain, usually very severe, which at the onset does not differ particularly from that of any appendiceal attack In referring back to the histories of these cases. Brunn finds that the pain may start in the epigastrium or around the umbilicus, but soon settles in the lower abdomen In the great majority of cases. the history is that of a well individual waking up suddenly at night with a severe abdominal pain that prevents sleep When localization of the pain takes place, it is more frequently on the left than on the right side In older individuals, diverticulitis must therefore be thought of, but in young people this seldom enters into the diagnosis While at times the pain may be on both the left and the right sides, or on the right side alone, in the author's series of cases it is more commonly complained of on the left, and this to Brunn is the first indication of a possible pelvic appendicitis

Vomiting may or may not ensue Many times it is brought about by an attempt to take some cathartic such as salts, but it is not persistent

Diarrhea should be mentioned also, not as a special symptom of pelvic appendicitis but rather to draw attention to the fact that diarrhea is not uncommon in appendicitis

The onset, therefore, is not different from that of any attack of appendicitis, and appendicitis is usually considered among the diagnostic possibilities. On examination, however, the findings are so atypical that reasonable doubt is

thrown on this diagnosis. Brunn finds practically always a normal temperature, an abdomen that is flat and soft, and a total absence of rigidity. In these cases he may go over the abdomen again and again, with deep palpation, without an expression of pain or tenderness on the part of the patient. On consultation, these facts are always brought out by the physician in charge, in justification of his delay. It does not seem to be general knowledge that there is such a group of cases with these negative findings

The fourth symptom which is often present in these cases, and usually overlooked, is irritation on urination. In most cases this point must be brought out by direct questioning and when so done the patient will recall that he did have irritation on urination for a few hours, and perhaps frequency. In some cases the symptoms of irritation are dominant, and there are several on the author's list where cystoscopic and ureteral examinations were made in search of a diagnosis, although in each case appendicitis was considered possible in the early stages

If the appendix is very low in the pelvis and underneath the bladder, there may be a rather constant desire to move the bowels,—so that Brunn considers these two symptoms of importance desire for urination, and desire to defecate.

On urine examination, red blood ceils are frequently found in the urine. Ten to 20 cells are common. We believe that the appendix in such cases is often placed near the ureter, causing irritation, and that this finding should not be used to estop a diagnosis of appendicitis as has frequently been done.

The blood count is one of the most important single factors in diagnosis. The white count is usually high, 15,000 to 20,000 with a high polymorphonu-

clear count In only a few of our cases has there been a low count, 8000 to 10,000. but in such cases the polymorphonuclear count has usually been high

We have, then, a patient who looks well, who gives a history of severe abdominal pain which after 12 hours has probably eased off, who has a normal temperature, a soft belly and absence of rigidity and tenderness, whose pain, when complained of, has localized itself usually in the left lower quadrant rather than on the right, who has had some symptoms either of urinary or rectal irritation, and who has a moderately high white cell count with an increased polymorphonuclear count

Rectal examination is now of first importance to verify the diagnosis of pelvic appendicitis. While at the present time such examinations are more frequently made than in the past, Brunn believes that many of them are really perfunctory. With the possibility of a pelvic appendicitis well in mind, this examination should be done thoroughly, preterably on a hard table. In a fat individual, it is difficult enough ordinarily, and with the patient in a soft bed becomes practically impossible would turther urge that one examination is not sufficient. When seen early, the tenderness may not be made out with definiteness, and rectal examination should be repeated at least once or twice a day until a definite finding is made In this way only can an early diagnosis be approached, and rupture of the appendix avoided

Attention should be drawn to the fact that tenderness on rectal examination is noted early in those cases in which the appendix is low down in the pelvis, and is difficult to elicit where the appendix is just over the brim of the pelvis. In these latter cases, symptoms of rigidity and tenderness near Poupart's ligament

come on fairly early, which helps in making a diagnosis

The second 24 hours usually show a gradual and very moderate rise of temperature If there has been no rise in the leukocyte count, there will be a definite rise in the polymorphonuclear count by this time, and if a Schilling count is made there will be found a distinct shift to the left The left-sided pain may persist, but rigidity may still be absent The severe pain usually diminishes, and the patient feels as if he should go to work, and resents being kept in bed Finally, when rupture occurs,—and this often is very sudden and unexpected,the picture changes instantly There is sudden severe pain, marked rigidity, and dullness over the right or left side, or both, and over the pubis,—all the signs of an intra-abdominal calamity

Tuberculous Appendicitis — E Thieme¹⁹ has encountered seven cases of so-called primary tuberculous appendicitis, in two of which tuberculosis elsewhere was found later The history and physical observations in these seven cases were essentially the same as in pyogenic appendicitis and the diagnosis was not made preoperatively. The prognosis was uniformly good Twenty cases of pulmonary tuberculosis in which operations for appendicitis have been performed were reviewed, the lesion was acute in 13 and recurrent in seven Of the 20 patients, six had tuberculous appendicitis, five of them were doing poorly preoperatively from their pulmonary standpoint Of the six, five are dead and the sixth is critically ill The extremely poor prognosis of tuberculous appendicitis in advanced, uncontrolled pulmonary disease is evident. The 14 cases of pyogenic appendicitis occurred in patients who were doing well from the standpoint of their pulmonary tuberculosis Their subsequent course has been such as to lead the author to believe that their appendicitis was unrelated to their tuberculosis and did not affect the course of that disease

Appendicitis in Children-In a review of all cases of acute appendicitis admitted over a period of five years to the Duke Hospital by Randolph Jones, Ir, and Elijah E Menefee,²⁰ the mortality rate in children under 15 years of age was found to be more than twice that in adults. All the cases admitted to the children's ward during this period, with a tentative or definite diagnosis of acute appendicitis, therefore were reviewed with the hope of clarifying the problem of diagnosis as well as learning the more important factors governing the mortality rate and drawing some conclusions as to the most effective method of treating the extremely ill patients During the five-year period covered in this report 202 children under 15 years ot age were admitted with the diagnosis of acute appendicitis In the same interval 49 children sent to the hospital by their family physicians with the diagnosis of acute appendicitis were discharged without operative treatment following a decision that appendicitis was not the cause of their symptoms

A resume of the pathology of acute appendicitis in children is beyond the scope of this report. However, it should be remembered that children probably have less general resistance to intra-abdominal infection than adults. Also a child's thin bowel wall tends to make the incidence of perforation more trequent, and when peritonitis has developed the short omentum of childhood is much less effective in keeping the infection localized than is the larger apron of the adult

Some appreciation of the difficulties encountered in making an accurate diagnosis of acute appendicitis in the child

may be obtained from a review of the disorders for which an appendectomy was done in this series of cases (Tables 1A, B and C). The incidence of acute appendicitis in infancy is relatively low and the frequency increases proportionately throughout childhood into adolescence In infants and children too young to cooperate with the examiner, the diagnosis must rest largely on objective evidence of intestinal colic and signs of peritoneal irritation, such as tenderness on palpation of the abdomen, and possibly the demonstration of rebound tenderness With older children the attack usually follows a pattern, the essential features of which are abdominal pain, nausea, vomiting, and tenderness over the appendix. Rebound tenderness over the appendix is a sign of especial importance and was present in over 90 per cent of the children in the authors' series having acute appendicitis Infrequently an attack starts with vomiting prior to any pain In 12 per cent of the patients the abdominal pain was localized in the right lower quadrant from the onset of the attack, and did not follow the usual sequence of originating in the epigastrium or periumbilical region and later localizing in the right lower quadrant

The data obtained from a study of 202 children 14 years of age and younger admitted to Duke Hospital with a diagnosis of acute appendicitis, are presented A review of the cases emphasizes the variety of the diagnostic problems presented by the child with abdominal pain No child in this series died who was seen by the surgeon within 24 hours of the onset of the attack, and the authors believe that any child who has persistent abdominal pain for six hours should be considered as having an acute intra-abdominal condition. With Lord Moynihan, the authors deplore the "philo-

CHILDREN UNDER 15 MARKS OF AGE OPERALED ON WHILE FULLITIEF DIAGNOSIS OF ACUTE APPENDICITIS 1930 TO 1935

| | Results | 115 Well 9 Died | 39 Well | 8 Well | | 2 | 1 Well | | 2 Well |
|-----------------|--|--------------------|---|--|---------------------------|-------------------------------------|-------------------|--------------------------------------|----------------|
| | Findings on Operation Procedure | | Glands in mesentery 39 | Appendectomy Kinks, bands, fecaliths obstructing lumen 8 | en- | Appendectomy 2 Normal appendix 1 | Appendectomy | Diverticulitis 1 Obstruction from | diverticulum 1 |
| 91 | Rectal Tenderness or Mass | 106 | 27 | w | 2 | | | - | |
| - | Rigidity | 65 | 17 | | - | | | | |
| - | Rebound Tender- | 114 | 9 | 3 | - | | | - | |
| | Abdominal (RLQ) Tenderness | 124 | 35 | 9 | 2 | | | 2 | |
| | Average Leukon i tes | 16,000 | 37 7 14,356 | 10,700 | 11,000 | 7.000 | • | 19,000 | |
| İ | -lagge lempera- ture | 38 | 37 7 | 37 7 | 37 8 | 37.8 | 5 | 38 7 | |
| | Duration of Stimp- tony Prior to Operation | 130 hours | 63 hours | 98 hours | 54 hours | tx nical | attack one | 42 hours | |
| - | Catharsis | 89 | 5 | + | | | | - | |
| 1 | Previous Macks | 21 | 74 | ır | - | • | - | - | |
| | វ ១យវយេខ | 113 | 18 | | | _ | 1 | 2 | |
| | - Nausa | 120 | 3.1 | ٥ | | • | - | 7 | |
| | The Training Pain | 124 | 36 | ∞ | 2 | - | - | 7 | |
| | Female | 48 | 20 | Ŋ | | | | | |
| • |) મુકાર | 7.6 | 19 | 3 | ~ | - | - | 7 | |
| | Zumber of Cases | 124 | 39 | ∞ | 2 | • | - | 2 | |
| CHIEDNE CONTROL | Final Diagnosis | Acute appendicitis | Total cases Mesenteric lymphadenitis | Appendiceal colic | Appendices with parasites | | Interval appendix | Meckel's diverticulitis | |

CHILDREN UNDER 15 YEARS OF AGE OPERATED ON WITH TENTATIVE DIAGNOSIS OF ACUTE APPENDICITIS 1930 TO 1935 TABLE 1B

| | - | - | | | | _ | | | | | - | - | - | - | | |
|--------------------------|----|-----|--------------|-------|---|---|---|------------------------------|------|--------|---|---|---|---|----------------------------------|--------|
| Acute salpingitis | 77 | | 4 | £ _ 3 | | | 4 | 4 73 hours 38 1 15,000 4 2 2 | 38 1 | 15,000 | 4 | 2 | 2 | 4 | 4 Acute salpingitis 4 | 4 Well |
| Pneumococcus peritonitis | 2 | . , | 7 | 2 2 | 2 | | - | 84 hours 39 4 9,000 2 2 2 | 39 4 | 000,6 | 2 | 2 | 2 | 2 | Peritonitis with normal appendix | 1 Died |
| | | | | | | | | | | | | | | | Appendectomy with drainage | 1 Well |
| Menarche | 3 | | 3 | 3 2 | | 2 | - | 33 hours 37 1 9,700 | 37 1 | 00,700 | 8 | 7 | | - | Normal appendix 3 Appendectomy 3 | 2 Well |
| Pyelitis | 2 | | | 2 1 | _ | 2 | | 64 hours 38 9 21,000 2 | 38 9 | 21,000 | 7 | ~ | - | - | Normal appendix 3 Appendectomy 2 | 3 Well |

(Courtesy, Am Jour of Suig, Sept, 1937)

TABLE 1C

| CHILDREY UNDER 15 YEARS OF | 3 15 YE | EARS | OF A | GE 01 | ERAT | ED ON | WITH | THE TENTATIVE | DIAG | NOSIS OF | , Acu | re Ap | PEND | AGE OPERATED ON WITH TENTATIVE DIAGNOSIS OF ACUTE APPENDICITIS 1930 TO 1935 | | |
|---|-----------------|-------|--------|----------------|-------------|---------------------------|-------------|---|--------------------------|---------------------|----------------------------|-----------------|----------------------------|---|----------|---------|
| Final Diagnosis | Number of Cases | blale | Female | Abdominal Pain | Nausea | Vomiting Previous Attacks | Catharsis | Duration of Symp- toms Prior to Operation | Average Tempera- stut | Average Leukocytes | Abdominal (RLQ) Tenderness | Rebound Tender- | Rigidity Rectal Tenderness | Findings on Operation Procedure | ration | Results |
| Abdominal pain with upper respiratory infection | 9 | 2 | 4 | 9 | ر د | 2 | 2 3 | 106 hours | 37.8 | 10,000 | 9 | 8 | 23 | 2 Normal appendix | | 6 Well |
| Abdominal pain | ıv. | | 4 | Ŋ | 2 | 7 | 2 1 | 80 hours | 3 37 7 | 11,000 | 25 | 4 | 8 | 3 Normal appendix | X N | 5 Well |
| Cause Undetermined Rheumatic fever | | | | - | | | | 6 hours | , 37 6 | 6 hours 37 6 19,000 | - | - | | 1 Normal appendix | | 1 Well |
| Catarrhal jaundice | | _ | | - | | - | | 31 hours | , 39 4 | 000'6 | | - | | 1 Normal appendix Appendectomy | X 1 1 | 1 Well |
| Pleurodynia | | | | | | | | 96 hours | 37 4 | 000,9 | | | | 1 Normal appendix | × | 1 Well |
| Gastroenteritis | — | | | - | | | | 216 hours 38 4 | s 38 4 | 11,000 | | | | Normal appendix Appendectomy | × | 1 Well |
| Total Tables 1A, B, C | 202 | 108 | 94 | | | | | | | | | | | | | |

(Courtesy, Am Jour of Surg., Sept., 1937.)

cathartic propensities" of parents and note also that opiates in children, as well as in adults, should not be given to relieve abdominal pain until after the diagnosis of the intra-abdominal condition has been made by the physician who is to carry the treatment to its conclusion. Emergency operations should not be done on children who have a widespread peritonitis until dehydration and acidosis have been corrected. The timely opinion of an able pediatric or medical consultant may help clarify a difficult diagnosis and avoid an unnecessary operation.

Because abdominal pain and vomiting are frequently early symptoms of the exanthems J G M Bullowa, E J McCade, and S M Wishik²¹ point out that appendicitis is overlooked occasionally in the early stages of those conditions On the other hand, children are operated on frequently in the prodromal stages of the various exanthems for conditions which turn out to be pseudoappendicitis. The differentiation between pseudoappendicitis and true appendicitis is difficult. The authors ofter no method for differentiation, but state that true appendicates is extremely rare in the prodromal stage of the exauthems and that when there is a history of exposure to disease as measles, right lower quadrant pain may be due to pseudoappendicitis unless the findings are overwhelmingly those of a condition requiring surgery. They believe that a specific giant-cell reaction of the exanthem can occur in the appendix and give pseudoappendicial symptoms They report 21 cases of definite appendicitis which were operated in 26,462 patients with contagious diseases

Appendicitis from Oxyuris—This is discussed by A Battaglia and H di-Fiore ²² They found that appendicitis is caused by oxyuris with a frequency

of two per cent It is more frequent in children than in adults Only two patients out of a group of 11 suffering from oxyuris appendicitis complained of symptoms of oxyuriasis (occasional dizziness with unconsciousness) A microscopic study of the removed appendix was performed in three cases. The appendix was the seat of chronic inflammation and typical oxyuris lesions The hemogram in three cases showed eosinophilia (four, five and eight per cent, respectively) The appendix was intensely parasitic (29, 62 and 83 oxyurids, respectively) The largest number of oxvurids isolated from the appendix were female The examination of the feces for parasites and of the lumen of the appendix for eggs gave negative results

Acute Appendicitis Past Middle Age—According to N renko²³ 2888 cases of acute appendicitis were admitted to the third surgical clinic of the Second Leningrad Medical Institute between 1919 and 1934 Of the patients, 410, or 142 per cent, were past 40 years of age An analysis of the incidence and of the clinical course of this group shows that acute appendicitis is almost as frequent in this age as in the younger persons. The onset of the disease exhibits less pronounced pain, and temperature reaction, nausea and vomiting are noted less frequently, the typical local tenderness at McBurney's point may be absent and the tenderness frequently extends beyond the right lower abdominal quadrant Atypical complaints and historical data further obscure the picture The leukocyte count is relatively lower than anticipated and occasionally leukopema may exist The pathologic alterations in the appendix are more pronounced and the percentage of perforations is high. The course of the disease is characterized by grave complications and a high mortality rate There is a frequent lack of relationship between the clinical symptoms and the pathologic observations Profound pathologic alterations may exist in patients with trivial complaints and apparently insignificant objective signs The high mortality index in the old depends principally on the rapid development of pathologic alterations On the other hand, patients operated on early give a mortality rate not much higher than that of the younger groups

Pylephlebitis—Pylephlebitis or mesenteric pyemia as a complication of appendicitis, according to A T Lidskiy24 is on the decrease. He believes that this is due to the more universal application of the principle of early operation in acute appendicitis. One or more chills, rise in temperature, icteric discoloration of the skin and of the sclerotics, enlargement of the liver and a blood picture characteristic of a severe acute suppurative process suggest the diagnosis The early diagnosis, however, is difficult and even liver puncture, as proposed by Nossen, Martens and other authors may in the presence of multiple small liver abscesses give negative results There exist few indications for ligation of the ileocecal veins at the time of appendectomy A secondary operation proposed by Wilms and having for its aim ligation of the ileocecal veins in order to arrest the spread of infection into the superior mesenteric vein, the portal vein and the liver has given encouraging results. To be effective it must not be delayed until the development of a characteristic clinical picture. The prognosis in the presence of this complication is grave, the mortality ranging with various authors from 80 to 100 per cent. The best prophylaxis is the early operation of acute appendicitis This indication becomes even more stringent in the pres-

ence of a chill in an acute case of appendicitis.

Chronic Appendicitis—There is a great deal of objection to designating chronic appendicitis as an idiopathic illness M Margottini²⁵ states that some consider it the result of a preceding acute inflammation; some admit its existence only when it accompanies disease changes in neighboring organs. Others wish to restrict the term to tuberculosis and actinomycosis of the appendix.

Guided by clinical as well as by histological criteria, the author reports that among 487 operations for appendicitis in the San Giovanni Hospital in Rome there were 33 cases (68 per cent) which were rightfully diagnosed as chronic appendicitis The symptoms were similar to those of the acute type but less severe, or they consisted of dyspeptic disorders, sometimes even simulating cholecystitis, chronic gastritis, or gastric ulcers In some cases pelvic symptoms, such as frequent urination or dysmenorrhea, prevailed Some cases showed absolute latency and the diseased appendix was revealed at operation for other reasons Histologically, the picture of chronic appendicitis was twofold hyperplasia of the lymph follicles, often with numerous eosmophile cells in the mucosa, or atrophy of the mucous membrane with obliteration of the appendix by fibrosis That the appendix really was the cause of the illness in these cases was demonstrated by the fact that 90 per cent of the patients were free from symptoms after the operation Therefore, appendectomy should be advised, when medical treatment does not give relief, especially as there is always the possibility of an acute flare-up of the chronic process The incision should be large enough to allow a thorough exploration of the abdomen Very often similar lesions affecting the last part of the ileum, the

cecum, or the adnexa of the uterus may be discovered

R. Rabboni²⁶ reports 40 cases of Leotta's right abdominal syndrome in patients under 15 years of age who were observed at the Surgical Clinic of Palermo during the last five years. He calls attention to the fact that chronic appendicitis in such young persons has been little studied. He discusses the relationship between chronic appendicitis and the simple right abdominal syndrome

The right abdominal syndrome is a chronic and periodical affection of the digestive tract due to a chronic inflammation of the appendix in children and adolescents. The symptoms are anorexia, nausea, eructation, constipation, and pain which is localized in the epigastrium and ileocecal fossa and diffused over the whole right half of the abdomen. In the first stage only the appendix is chronically inflamed. Later the peritoneum becomes inflamed

Operation should be performed as early as possible for if the condition is neglected in children and adolescents it may develop later into the more severe and complicated forms of right abdominal syndiome in adults, such as cholecystitis and gastroduodenal ulcer. Operation was done in 18 of the 40 cases reviewed by the author

In conclusion Rabboni says that the right abdominal syndrome has been confused with dyspeptic disturbances, ordinary gastritis, and the most varied diseases of the gastrointestinal tract

During the past few years, M Feldman²⁷ has encountered a large number of adult patients on whom an appendectomy had been performed for so-called *chronic appendicitis*, without relief of their symptoms. A thorough painstaking roentgen examination of the gastrointestinal tract, gallbladder, colon and

genito-urinary tract, including cystoscopic and pyelographic studies when indicated, is necessary in every case of suspected chronic appendicitis In a study of 115 cases of so-called chronic appendicitis, following removal of the appendix, the roentgen examination revealed pathologic conditions other than in the appendix, which accounted for the gastrointestinal disturbance. Peptic ulcers accounted for 365 per cent of the dis-. orders, pathologic states of the gallbladder for 26 per cent, and the genitourinary tract was involved in six per cent. The differential diagnosis of chronic appendicitis is almost impossible without the aid of roentgen studies, by which means a large number of conditions producing gastrointestinal symptoms that closely mimic appendiceal disease may be ruled out In no instance should operative measures be undertaken for chronic appendicitis until all other conditions have been eliminated. The roentgen method of investigation is of the greatest importance as an aid in the ultimate diagnosis

Mortality—The operative mortality for acute appendicitis as reported by H. J. King²⁸ under a régime of radical treatment as practiced by a sizeable group of surgeons employing varied technics, was 42 per cent during the year 1934 to 1935. This represents a marked reduction in the mortality of five years previously. While this mortality in no sense is comparable to that reported by certain clinics, better hospitals, and in various individual series, it nevertheless represents a rather respectable effort to cope with a problem of increasing difficulty

Inadequate hospital records prevented an evaluation of the importance which the factors of time and cathartics may have played in effecting this lowered mortality, but it is certain that better surgical judgment and improved surgery were largely instrumental in producing the marked drop in mortality which occurred in the group of cases complicated by peritonitis.

The mortality in acute uncomplicated appendicitis in the author's institution is creditable and probably almost irreducible, but the treatment of appendicitis with abscess still shows a mortality which is much too high.

No one operative procedure will effect a material drop in mortality among the severe cases of appendicitis. Improved mortality in all probability will result largely from the exercise of better judgment as to when to operate and how much to do However, three points in operative procedure do stand out as worthy of particular consideration in any plan for reducing operative mortality in appendicitis

- 1 The weight of evidence seems to indicate that in the very small percentage of cases where a severe spreading *pertonitis* complicates the picture, a régime of conservative treatment and temporary delay in operation offers the patient the best chance of recovery
- 2 Controlled series seem to show that the use of the McBurney incision or its modifications favors a lowered mortality by confining operative manipulations to a very limited area of the abdomen, thus helping to keep the peritoneal infection localized
- 3 In an admittedly short series of cases, bacteriophage has shown that it is worthy of further investigation in the treatment of cases complicated by peritonitis

The experience has been that improvement in the hospital management of acute appendicitis is capable of producing a marked lowering in the mortality rate of this disease. It appears probable, however, that any considerable mortality drop will occur only when the public

is thoroughly enlightened regarding the dangers of catharsis and of procrastination in the treatment of abdominal pain, and when routine early hospitalization of these cases will make possible removal of the appendix at a time when the operation carries with it, in experienced hands, a mortality which is almost negligible.

R. D. McClure and W. A. Altemeier²⁹ studied 252 consecutive cases of acute perforated appendicitis which were treated at Henry Ford Hospital during the period from 1915 to 1933 with special reference to the mortality rate. In 221 per cent of the patients admitted with acute appendicitis, perforation had occurred. The cases were divided into four groups

Group A. Cases with perforation of the appendix and local peritonitis. These made up 21 83 per cent of all the cases, and showed no mortality.

Group B Cases with perforation of the appendix and abscess formation. This group made up 46 43 per cent of all the cases, and showed a mortality of 42 per cent

Group C Cases with perforation of the appendix and general peritonitis. These amounted to 25 79 per cent of all the cases, and showed a mortality of 21 5 per cent

Group D Cases with perforation of the appendix, general peritonitis, and abscess The mortality in this group was 46 6 per cent

During the 19-year period from 1915 to 1933 the operative mortality decreased from 22 2 to 7 7 per cent

The authors analyzed their series very carefully as to the predisposing and exciting factors of the conditions. An analytical study was made of the bacteriology, pathology, symptomatology, and treatment. In view of the mortality rate reported it is interesting to note that

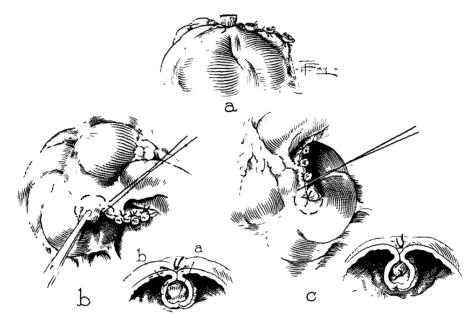
"it has been the rule in the authors' clinic to operate immediately after the diagnosis of acute appendicitis has been made regardless of the duration of the symptoms unless the patient is practically moribund."

The *McBurney incision* was used in 70 per cent of the cases and is now favored by the authors as a routine procedure. Unless specifically contra-

Jr, and R A Daniel, Jr ³⁰ These patients were admitted to the Vanderbilt University Hospital between the years 1925 and 1935, inclusive

The mortality rate for the entire group 13 51 per cent, six patients who were not operated upon being excluded

Of the 686 cases of unruptured acute appendicitis, there was one death, a mortality rate of 0 145 per cent



Ing 10—Various methods employed in handling the appendical stump a, Simple ligation of the stump which is left tree in the peritoneal cavity, b, inversion without ligation of the stump. Purse string suture is placed in such a way as to encircle the intramural branch of the appendical afters. The stump which has been crushed by three clamps is divided between the upper and middle clamps, leaving two clamps on the stump, thus permitting grasping of the appendical stump by means of the inverting forceps before the proximal clamp has to be removed. The unligated stump is inverted into the occumal. The ligation and inversion technic following introduction of the pursestring suture in which the appendical stump is ligated and inverted into a closed cavity in the occal wall. (Courtess. Surgery, Oct. 1937.)

indicated, spinal anesthesia is used. The use of the McBurney incision and spinal anesthesia, together with careful preoperative and postoperative treatment, in the opinion of the authors, account for the declining death rate from perforated appendicitis.

A study of 1000 consecutive patients in whom a diagnosis of acute appendicitis was made, is presented by J. A. Kirtley,

Of the 30 cases of ruptured appendicitis in which operation was performed there were 50 deaths, a mortality rate of 163 per cent

The mortality rate and incidence of ruptured appendicitis are highest at the two extremes of life

In approximately one case in every three, the appendix was ruptured at the time of admission In more than half of the cases of ruptured appendicitis, the patients had received catharsis before admission.

Treatment — A Ochsner and G Lilly ³¹ point out that as early as 1895, three basic methods of handling the appendical stump were used. Since this time each of the three methods has been championed by many eminent surgeons,

The inversion without ligation of the appendical stump overcomes the objections to the other two technics in that (1) The serosa is brought in apposition to serosa, thus insuring firm healing of the cecal wound and obviating the danger of subsequent leakage from the cecum and peritoneal contamination; (2) contamination is prevented from an infected

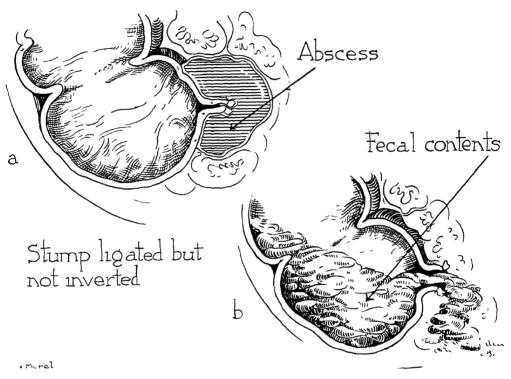


Fig 11—Diagrammatic drawing illustrating what probably happened in Case 1. As shown in a, an abscess developed around the ligated stump, which resulted in weakening of the ligated stump and infiltration of the cecal wall. Following administration of the enema, the ligated stump blew out, permitting escape of tecal contents from the lumen of the cecum into the peritoneum, b, resulting in a tatal peritonitis. (Courtesv. Surgery, Oct., 1937.)

and it is the purpose in this presentation to attempt to evaluate each method (1) Simple ligation of the stump (Fig 10 a), (2) ligation and inversion of the stump (Fig 10 c), and (3) inversion without ligation of the stump (Fig 10 b) The advantages and disadvantages of the three technics should be considered from the standpoints of (1) technic and (2) anatomic and physiologic principles

stump lying free in the peritoneal cavity, (3) careful peritonealization is secured, and (4) the infected appendical stump is not buried in a closed cavity. As shown by the experimental investigations of Burkle-de la Camp, the inversion without ligation of the appendical stump results in perfect healing of the cecal wound without any necrosis, exudation beneath the serosal sutures, or inflam-

matory infiltration. The lack of findings following this type of operation contrasts favorably with the marked inflammatory reaction occurring at the site of the ligated and inverted appendical stump.

After a thorough consideration of all phases of the question it is obvious that there is no justification for ligation and inversion of the appendical stump. This method seems to combine all that is

reaction can be the origin of peritoneal adhesions, as emphasized by Kohler and others On the other hand, Ochsner and Lilly do not feel that the simple ligation method is desirable because of the very definite danger that the ligature may come loose and slip off or cut through the crushed appendical stump, as in Case 1. Simple ligation of the stump is also undesirable because of the high incidence of other complications following

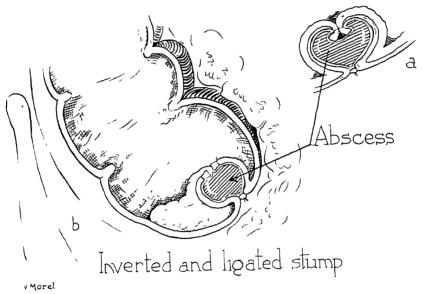


Fig. 12—Diagrammatic drawing showing probable occurrence in Case 2. As shown in insert a, an abscess developed around the inverted and ligated stump which caused the patient's elevation of temperature and tumefaction in the right iliac fossa. Fortunately, as shown in b, the abscess ruptured into the cecil lumen, the pus being evacuated from the rectum, resulting in complete recovery (courtesy, Surgery, Oct., 1937.)

objectionable in the other two and has nothing to recommend it. The authors feel that the probability of the development of a cecal wall infection without adequate drainage is sufficient reason for an unqualified condemnation of this procedure. The almost invariable development of an acute inflammatory reaction at the site of the ligated inverted stump is a potential cause of peritonitis which may end fatally, as in Case 3 Even though actual suppuration occurs infrequently, the milder types of inflammatory

It, as illustrated by Willis' investigation. Twenty-one per cent of 105 surgeons stated they had observed complications which consisted of fecal fistulas, adhesions to the ligated stump producing obstruction, and peritonitis. The authors do agree with Gurd, however, that when the cecal wall is indurated and edematous, simple ligation is the only practical procedure, because of the difficulty and frequent impossibility of inverting the appendical stump. That it is the only procedure possible in such cases does not

justify its use in other cases in which inversion can be accomplished.

The only objections that can be made to the use of the inversion without ligation method are: first, the danger of the stump opening and causing contamination before it can be inverted; second, the danger of traumatizing or perforating the cecum while installing the pursestring suture; and third, the danger of postoperative bleeding into the cecum

of these two clamps is removed and the crushed end of the appendical stump is grasped with a pair of plain-tipped tissue forceps before removing the proximal crushing clamp. After the crushed end has been conveniently and securely grasped, the first clamp is removed and the stump inverted into the cecal lumen without any spillage or contamination, because the crushed stump remains temporarily sealed.

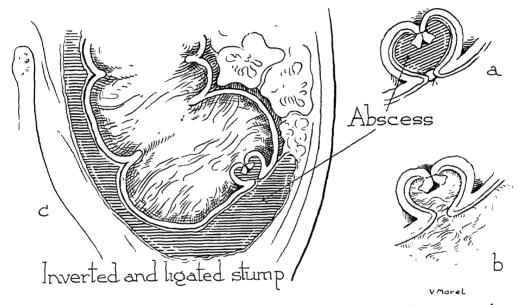


Fig 13—Diagrammatic drawing of probable occurrence in Case 3. As shown in a, an abscess probably developed around the inverted, ligated stump. As shown in b, this perforated to the outside, resulting in a pericecal abscess, which extended up lateral to the colon as shown in c. (Courteev Surgery, Oct. 1937.)

from an intramural artery in the appendical stump. As regards the first objection. The authors feel that contamination can be avoided easily by the employment of the described technic. They do not feel that the use of special crushing and inverting clamps, as advocated by Kelly, and recently modified by Al Akl, is necessary or desirable. They have found that the stump can be sufficiently sealed by applying two Ochsner clamps proximal to the site of removal (the third distal clamp is removed with the appendix). The distal one

The danger of producing a hematoma in the cecal wall or perforating the lumen while installing the purse-string suture is a theoretical one and can be obviated by the careful introduction of the suture. If a fine silk suture on an atraumatic needle is used, the amount of trauma to the cecal wall is negligible. There is no reason why the cecal wall should be traumatized more or a hematoma caused more frequently in inverting the appendical stump than in the inversion of the duodenal stump or other intestinal stumps, which is considered by all sur-

geons the only proper way of managing such conditions.

The danger of postoperative hemorrhage from an intramural branch of the cecal artery in the appendical stump is a definite one, as has been pointed out by Seelig, unless measures are used to prevent its occurrence. As all the blood orrhage from the unligated stump Other cases of hemorrhage have been reported by Fowler and Seelig Hemorrhage from the stump in such an instance must come from an intramural branch of the appendicular artery which was not secured by ligation of the mesoappendix. In anatomic investigation the authors found, in

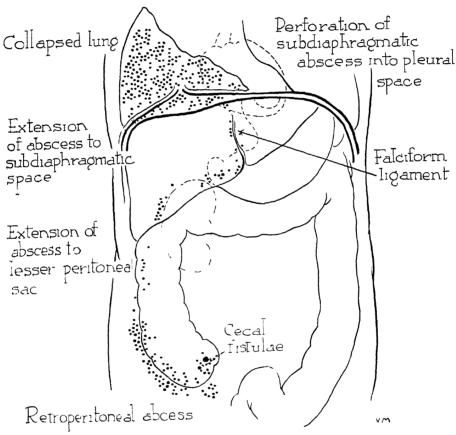


Fig. 14—Case 3. Diagrammatic drawing showing extension of infection from cecal fistula up along the lateral aspect of the colon to the subphrenic area and by perforation through the diaphragm into the pleural cavity. (Courtesy, Surgery, Oct., 1937.)

supply to the appendix is derived from the appendicular artery, which is located in the mesoappendix, it is reasonable that ligation of the latter would result in complete hemostasis in the appendix. Hemorrhage from an unligated stump has been reported by many observers. In the statistical study made by Willis, ten of the 105 surgeons who responded to his questionnaire stated they had observed hem-

15 per cent of cadavers examined, an intramural branch of the appendicular artery which would not be caught if the mesoappendix alone was ligated. Complete hemostasis can be secured in such cases by introducing the purse-string suture in such a way as to obliterate an existing intramural vessel. The introduction of the purse-string suture begins at the attachment of the mesoappendix

and passes through the cecal wall at this point down to and including the submucosa Instead of continuing around the base of the appendix in the conventional manner, the needle is inserted a second time at the mesenteric attachment, making a loop around that portion of the cecal wall. This accomplishes the same purpose as the purse-string suture-

the inversion without ligation technic, the dangers of the other two methods cannot be entirely eliminated and although in most instances the patient will recover from an appendectomy performed according to the simple ligation and ligation plus inversion technics, the morbidity is likely to be greater and cause more frequent complications. The possibility

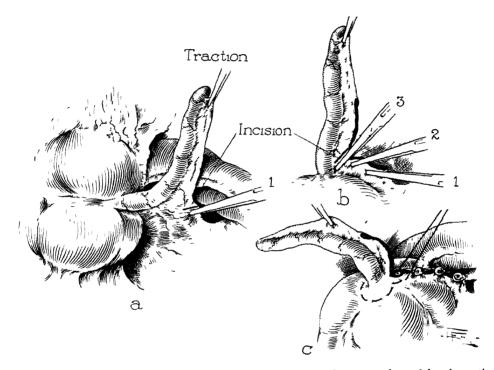


Fig. 15—Method of division and ligation of the mesoappendix, as performed by the authors λ s shown in a, the mesoappendix is not clamped or ligated en masse, but is caught with small forceps and each area divided and ligated individually. Following division and ligation of the mesoappendix a purse-string suture is placed around the base of the appendix as in c (Courtest, Surgert, Oct. 1937)

ligature described by Nixon, but the authors feel that the method described has the additional advantage of affording a fixation of one end of the purse-string suture, and thereby facilitates the inversion of the stump. Because the theoretical disadvantages of the inversion without ligation method can be overcome easily by the technic suggested and because this technic satisfies all physiologic and surgical requirements, it is the ideal technic of appendectomy. In contrast to

of occasional, but fortunately rare, catastrophes, as in the three cited cases, should preclude the use of either of the last two technics as they are neither surgically nor physiologically sound

The author concludes that appendectomy should be performed while the inflammation is still confined to the appendix and in such a way as to prevent contamination of the peritoneum and the abdominal wall either during or after operation and also in such a way that no

hemorrhage can occur from the appendical stump.

Simple ligation of the appendical stump prevents the burying of the infected stump in a closed cavity, secures hemostasis, and is easily performed. The procedure, however, is unsurgical, because there remains free in the peritoneal cavity a contaminated raw surface Con-

"blowing out" of the appendical stump treated by simple ligation is reported.

Ligation and inversion of the appendical stump is the technic most frequently employed. It has the advantage that peritonealization and hemostasis are secured. The method, however, violates a surgical principle, i e, the inversion of an infected stump into a closed cavity. As

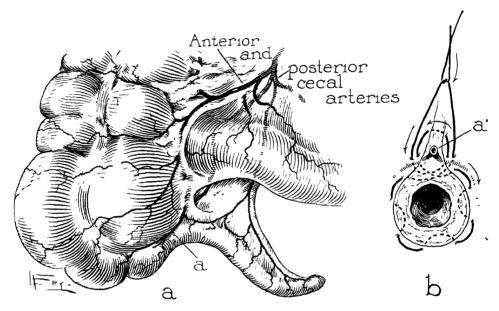


Fig 16—a, Blood supply of the appendix derived from the anterior and posterior cecal arteries, b, method of introducing a purse string suture in such a way as to include a possible inframural branch of the appendicular artery, a' As illustrated in the drawing, the purse-string suture is begun at the antimesenteric attachment, passes through the submucosa at the base of the appendix, and emerges on the opposite side of the mesoappendix. It is carried over to the beginning side and reinserted so that a loop as shown by the arrow, is made around any inframural branch of the appendicular artery. The purse-string suture is then carried around in a conventional manner back to the mesoappendix. In this way the possibility of hemorrhage from an inframural branch of the appendicular artery is prevented. (Courtesy Surgery, Oct., 1937.)

tanimation of the peritoneal cavity may result from the ligated stump either from the micro-organisms on the stump or because of loosening of the ligature or necrosis of the stump as a result of the ligation Simple ligation of the stump does not secure apposition of serosa to serosa which is important in all gastrointestinal surgery. The incidences of fecal fistulas, persistent sinuses, peritonitis, and intestinal obstruction are high following this method. A fatal case of peritonitis from

a result of inflammation occurring around the inverted, infected stump, there is likely to be extension of the inflammatory process to the surface of the cecum with resulting peritoneal reaction and adhesions. There is also likelihood of an abscess forming which may resolve spontaneously, rupture into the cecum, or into the peritoneal cavity. Two cases are reported, one which recovered, in which presumably a cecal wall abscess ruptured into the lumen of the cecum and

the other in which the abscess ruptured into the peritoneal cavity, resulting in death. As a result of the ligation and inversion, granulomas can develop at the site of the stump and cecal diverticula have been reported.

dical stump and by grasping the crushed sealed stump before the last forceps is removed prior to inversion. Hemostasis is then secured by introducing a pursestring suture in such a way that an intramural branch of the appendicular

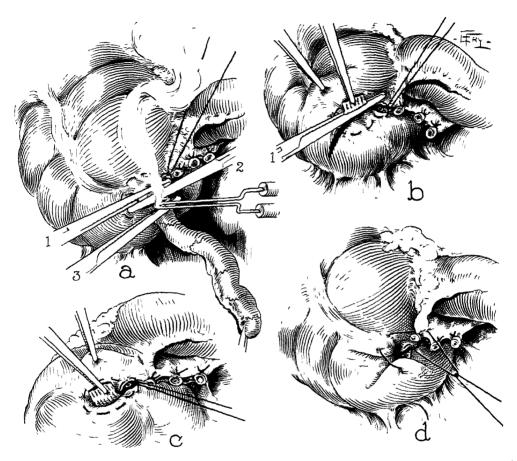


Fig 17—Technic of appendectomy a, After introduction of the purse-string suture in such a way as to include any intramural branch of the appendicular artery, three crushing clamps are applied to the base of the appendix, and the appendix is divided between the upper (3) and middle (2) clamps, b, the upper (2) clamp on the mesoappendix is removed, permitting the operator to grasp the crushed end of the appendix before the lower (1) clamp is removed. In this way the danger of spillage during inversion is obviated, c, inversion of the unligated stump into the cecum, following which the purse-string suture is tightened, d, further inversion of the inverted stump is accomplished by the introduction of several Lembert sutures over the inverted stump, and as a final procedure the ligated mesoappendix is sutured over the inverted stump, thus peritonealizing the entire area (Courtesy, Surgery, Oct., 1937)

The inversion without ligation technic is the ideal procedure provided that the stump can be inverted without contamination of the peritoneal cavity and that hemostasis can be secured. In the technic described this is accomplished by applying three crushing forceps to the appen-

artery is grasped in the purse-string suture. Because the crushed stump is inverted into the lumen of the cecum, there is no danger of subsequent inflammation occurring around this stump and extending to the cecal wall or peritoneal cavity.

Appendiceal Infiltrations and Abscesses

Treatment - During the past 25 years, W F. Suermondt 32 holds that in acute appendicitis without extension to adjacent structures and in appendicitic diffuse peritonitis the appendix should be removed at once, whereas in cases of appendicitis infiltrations and abscesses the treatment should be conservative because the body has already walled off the infectious process from the rest of the peritoneal cavity and if appendectomy is done at once the adhesions will be separated by the operation and the previously encapsulated peritonitis may become generalized Another danger of immediate appendectomy in cases of the latter type is the formation of spontaneous postoperative fistulas Therefore all depends upon whether the disease has reached the stage of infiltration when the patient enters the hospital. The 48-hour limit is no longer considered an important factor in the indications for operation. If a patient with all the signs of an acute progressing appendiceal inflammation is admitted to the hospital after 48 hours, immediate operation is performed. If, on the other hand, a patient is admitted with a palpable infiltration in the appendecal region within 48 hours, operation is delayed. The transition between infiltration and abscess is gradual. Therefore no sharp differentiation is made between infiltration and abscess with regard to the indications for operation

The patient with appendicitic infiltration is placed at absolute rest in bed in bowler's position and treated by the application of an icebag and diet. The extent of the infiltration is ascertained at the time of his admission. If the infiltration subsides by resorption, operation is performed six weeks later. If an abscess forms, operation is done only if the abscess points upward or medially;

that is, toward the free peritoneal cavity. Extension downward is not an indication for operation The three forms of spontaneous rupture - into the rectum, the vagina, and the bladder—are not serious complications At the subsequently necessary operation, an incision giving good exposure, such as the pararectal or the long gridiron incision, is essential operation is done because of extension of the abscess, the abdomen is merely opened and drained, the appendix is never sought In each of six cases a spontaneous intestinal fistula developed following the incision of an appendiceal abscess, but in each it closed spontaneously

The results during the past 25 years are summarized as follows

- 1 In 2853 cases of acute appendicitis without or with free, nonencapsulated peritonitis which were treated by immediate operation, there were 77 deaths, a mortality of 27 per cent
- 2 In 40 cases of acute appendicitis with encapsulated peritonitis, which were treated conservatively there were three deaths, a mortality of 0.7 per cent. In 256 cases in which only expectant treatment was given, there were no deaths, and in 151 in which the abscess was opened, two deaths. In 405 cases in which a secondary appendectomy was done there was one death, a mortality of 0.3 per cent.
- 3 In 778 cases of chronic appendicitis in which operation was performed there were two deaths (two from chloro form in the years 1911 and 1913)

Of the three deaths in Group 2, one was probably due to a technical error. The others were those of patients who were in such poor condition at the time of their admission to the hospital that they probably could not have been saved by any treatment. Of the patients in Group 1 who were treated during the

first ten years of the reviewed period, 50 (79 per cent) died, whereas of 2223 of this group who were treated during the last 15 years, only 27 (12 per cent) succumbed

In the author's opinion, conservative expectant treatment of appendicitis abscesses and infiltrations yields better results than immediate appendectomy. The mortality of radical treatment is given by Abel as 4 05 per cent, by Rieder as seven per cent, and by Stich as 5 1 per cent

COLON

Diagnosis—Inflammatory lesions of the colon are receiving more consideration. Articles dealing with circumscribed phlegmons of the cecum which may or may not be associated with similar lesions in the ileum are summarized in the 1937 edition. It is believed that these lesions should be excised by a more or less radical procedure, if spontaneous recession does not occur as there is a strong tendency toward chronicity and fistula formation.

The treatment of ulcerative colitis is stressed in a report dealing with 149 cases at the Massachusetts General Hospital Ileostomy, eccostomy or appendicostomy are surgical measures used to afford rest to the affected bowel, combined with supportive treatment. Many of the surviving patients will later require subtotal colectomy for complete relief

An important contribution dealing with carcinoma of the colon shows that the symptoms and signs of carcinoma of the right half of the large intestine are not diagnostic but suggestive. They are Pain, localized to the right side, vague indigestion, anemia, change of intestinal habit, a tumor mass, and occult blood in the stool. Signs and symptoms of the

left half of the colon are. Obstruction, either complete or partial; change of intestinal habit, tending toward progressive constipation; blood and mucous in The tumor mass is not so the stool often found Physical methods, particularly palpation, digital exploration of the rectum, and x-ray examination are of utmost importance in diagnosis Promising results are offered where early radical surgical treatment is instituted. The results show only 40 per cent operability in cases presented, but follow-up studies show that 66 per cent of cases were free from recurrence after five years, when early radical operation was performed

Next to ignorance of its cause, tardiness remains the greatest obstacle in combating cancer of the rectum and colon G G Stebbins and Meade Burke33 point out that tardiness may involve the patient, the physician, or the cancer itself In the mind of the average patient, cancer still manifests itself more as a visible or palpable growth than as an impaired function He is not apt to connect it with a mere change in bowel habit Consequently, he is tardy in seeking medical aid His physician may neglect making a digital examination, and be tardy in diagnosis Again, the cancer itself, by its failure to cause pain early, may be responsible for the tardiness. When it is recalled that cancer of the rectum and colon often grows slowly and metastasizes late, the record of these 295 cases seems even more distressing

A few of the principal tabulations set forth in the chart may be mentioned briefly

Of the 295 cases of all types, only 125 were referred here with the correct diagnosis, although the tumor was palpable in 180 cases, and constitutional signs present in 201 In 216 cases, one or more of the following factors had been pres-

TABLE 2

CANCER OF THE RECTUM AND COLON—WISCONSIN GENERAL HOSPITAL—OCT 1924 TO OCT 1935

| Location of Cancers | Rect | tum | R Junc and Si | tion | Col | on | Cec | um | |
|--|-----------------|----------------|---------------------|--------------|---------------|--------------|---------------|--------------|------------------|
| Nature of Cases | Clini- cal | Au- topsy | Clini- cal | Au- topsy | Clini- cal | Au- topsy | Clini- cal | Au- topsy | Total |
| Number of Cases | 117 | 46 | 60 | 6 | 27 | 16 | 17 | 6 | 295 |
| How referred here Correctly as cancer Incorrectly as something else. For diagnosis, or unknown Entrance history showing Tardiness in seeking medical aid, and/or | 63 15 39 | 20 10 16 | 19 11 30 | 3 2 1 | 3 8 16 | 5 4 7 | 9 2 6 | 3 1 2 | 125 53 117 |
| Tardiness in early diagnosis, and/or Inadequate early treatment | 88 | 36 | 42 | 4 | 16 | 10 | 15 | 5 | 216 |
| Entrance condition showing Primary cancer palpable Metastasis palpable Anemia, weight loss, cachevia | 102 13 86 | 32 8 31 | 10 2 34 | 4 1 5 | 10 0 18 | 8 1 10 | 11 2 14 | 3 1 3 | 180 28 201 |
| Nature of treatment possible Radical—attempt to cure Palliative—medical or surgical | 53 64 | 12 31 | 11 25 | 1 4 | 11 11 | 8 8 | 11 6 | 3 1 | 110 150* |

^{*}Treatment of remaining 35 cases Left or died before treatment, 8, refused treatment, 10, here tor diagnosis only 14, miscellaneous, 3 (Courtesy Am J Surg, Sept, 1937)

ent Tardiness in seeking aid, tardiness in early diagnosis, and inadequate early treatment. Of these three factors, tardiness in diagnosis occurred most frequently

Of the 163 cases of rectal cancer, only 83 were referred to the hospital with the correct diagnosis although the tumor was within reach of the index finger in 134 cases

With one exception, no appreciable difference was found between the records of clinical (morbidity) groups and autopsy (mortality) groups, although one might reasonably expect the former to be less distressing. The one exception lay in the number of radical operations in the two groups with cancer of the rectum, relatively more attempts to cure were made in the clinical than in the autopsy group

Patients with cancer of the cecum established a number of interesting rec-

ords They entered here with relatively the greatest number of (1) previous operations (usually for appendicitis), (2) correct diagnoses (usually because of the attempted appendectomies), and (3) histories revealing tardy diagnoses or inadequate early treatment. However, they were the only group of patients on whom radical surgery (attempt to cure) was possible in more than 50 per cent of the cases.

Carcinoma of Colon

Diagnosis—For the most part, carcinoma of the intestine may be diagnosed with greater ease, removed with less disability, and offers greater promise of cure than that of any other internal organ W. W Babcock³⁴ states that while three per cent occur before the age of 20, the great majority of intestinal carcinoma arise during middle life and attract attention chiefly by causing melena with

constipation or, less frequently, diarrhea. The bleeding is often attributed to hemorrhoids, but the blood is less in amount, often darker, more offensive and more intimately mixed with the stool. One out of eight of the cancers leads to an acute obstruction so that cancer is a common cause of ileus in the middle-aged and elderly

Often the patient is ruddy and robust during the first year or two of the disease, early anemia and cachexia being rare except with cancer of the cecum

The greater number of the cancers of the bowel are found in the rectum or lower sigmoid and may be felt by the finger in the rectum or seen through the proctoscope For the most part, the findings on palpation are diagnostic, an ulcer crater with hard, raised, everted and infiltrating borders so unmistakable in the average case that a biopsy to confirm the diagnosis is unnecessary. Unless made with care, a biopsy may perforate the thinned intestinal wall

In 60 per cent the patient is a man, usually between 45 and 60 years of age Chronic irritation of the intestinal wall as from acid secretion, high bacterial count, adenomas, polyps, proctitis, diverticulitis, chronic constipation or diarrhea are favoring factors

Carcinomas involving the colon above the pelvis are often palpable through the anterior abdominal wall. However, the annular scirrhous growths of the left half of the colon form a groove-like constriction of the bowel with so little mass that the growth may not be readily located even with the finger in the abdomen. For these small growths, roentgen studies with the aid of a barium enema are of great value. The expert roentgenologist will rarely be deceived by constrictions in the lumen from adhesions, benign strictures, diverticulitis, or regional ileitis or to pressure from without the bowel as

by abscess or solid masses. It is to be remembered that cancers of the lower bowel so easy to reach and diagnose by the finger are rarely shown on the x-ray film Cancer of the small bowel is rare and constitutes only two or three per cent of all intestinal carcinomas

With facilities for an early and positive diagnosis so readily available it is a reproach to our profession that many of these patients are permitted to drift on for months or even years assured, by a diagnosis such as "piles," "spastic" or "atonic colon," "colitis," "adhesions," that they are free from malignant disease. Yet even though the disease has existed a year or more before the diagnosis is made, in from 40 to 60 per cent of the patients it remains possible to excise the growth But it should be quite possible to diagnose the disease in at least 80 per cent before metastasis has occurred

No other internal cancer is so amenable to operative cure and with early diagnosis and sufficiently radical operation, the possibility of raising the percentage of surgical five-year cures from 40 to 70 or 80 per cent is within reason

Varieties (a) Scirrhous carcinoma occurs as a small inconspicuous, constricting growth in the narrower portions of the large bowel (the left colon), that is, from the middle of the transverse colon to the ampulla of the rectum. It produces obstructive symptoms, such as constipation, distention, borborygmus, visible peristalsis, or an acute ileus

(b) Adenocarcinoma, a more bulky fungating, ulcerating tumor, grows in the more expanded portions of the bowel, such as the cecum, ascending colon and ampulla of the rectum, usually produces diarrhea, or less frequently obstruction. An early morning diarrhea is an almost pathognomonic symptom of cancer of the ampulla of the rectum

(c) Papillary carcinoma is rather rare but grows large. It occurs especially in the rectum and anus, and causes profuse, watery and mucous dejections

(d) Colloid carcinoma also is relatively rare and is characterized by a spindle-shaped mass, annular constriction and tendency to metastasis

Treatment-For cancer of the intestinal tract irradiation has for the most part been very disappointing and rarely is to be advised at any time during the treatment The evolution of the surgical treatment of carcinoma of the intestinal tract has often been circular or backward, that is, supposed advances have merely been the adoption of forgotten or discarded procedures of former days Thus the author has abandoned many of the later anastomotic operations and returned not merely to the Mikulicz proedeure of 1902, but to the pre-Mikulicz procedures of Block of 1892 and Paul of 1895 for their freedom from peritoneal contamination

Stage operations have largely supplanted the one-stage operation for most resections of the colon Personally, Babcock no longer finds need for a permanent colostomy when it is possible to enucleate the intestinal carcinoma and for seven years has not employed it in such a case. The stage operations have been simplified and the hospitalization of patients much reduced. For carcinoma of the colon without acute obstruction, the preparatory treatment is very simple and consumes but a few days. A careful physical and laboratory study is made and if the patient is dehydrated or starved, an adequate supply of fluid and soluble nonresidue food, largely carbohydrate in character, is given Heavy purgation is avoided Repeatedly the author has seen a single dose of castor oil or a heavy meal produce an acute obstruction It is, of course, considered

desirable to have the colon as free from liquids or solids as possible at the time of operation With an intestinal obstruction, appendicostomy or cecostomy is immediately done and the radical operation delayed for two or three weeks until all peritoneal irritation has subsided. If the appendix is of fair size, an appendicostomy is preferred A 3 or 4 cm muscle-splitting incision is made, the appendix delivered and brought out through gauze dressings The tip of the appendix is then cut off and the largest catheter that can be introduced into the cecum is inserted and tied in With a small buttonhole incision no stitches may be necessary and in any case the mesoappendix must not be divided or compressed With a 20 cc Luer syringe, the injection and aspiration of warm saline are persisted in until the colon is decompressed This should not annoy the patient if he is well covered and in a comfortable position in bed Daily without disturbing the deep dressings, the catheter is withdrawn and larger sizes, thoroughly lubricated, introduced though the first catheter were only a 12 F, it often is possible to progress so rapidly that at the end of a week a rectal tube, size 28, is in place. If the appendix 15 found to be atrophic or bound down, a part of the cecum is withdrawn, clamped, gauze dressings applied under the clamp, and a mushroom catheter tied in by purse-string sutures distal to the non-traumatizing clamp which is then removed As a protective antiseptic varnish, Babcock moistens the gauze dressing with the compound tincture of benzoin

In the absence of obstruction, the diseased segment of the bowel is removed at the first stage by a modification of the old operation of Paul and Block Spinal anesthesia reinforced by the injection of the abdominal wall with 100 to 200 cc

of one per cent procaine solution containing one minim of epinephrine to each 10 cc. is used. For spinal anesthesia in these patients, Babcock prefers 100 mg of procaine in ten per cent solution combined with 4 or 5 mg of pontocain so that the analgesia will last two hours or longer. The local anesthetic solution supplies a bulk of fluid with the stimulant epinephrine in sufficient dilution to be slowly ab-Or under the brief anesthesia sorbed produced by the intravenous injection of evipal or pentothal sodium, the abdomen is quickly opened and adequate splanchnic and local anesthesia produced by the free injection of a one per cent of procaine with 1 60,000 epinephrine. Often the patient will then doze on almost oblivious of the operation for one or two hours

Types of Incision Employed-In resection of the cecum and ascending colon and especially the splenic flexure and lower end of the descending colon, the bowel has such deep attachments that it cannot conveniently be liberated and especially exteriorized through a vertical transrectus incision Babcock has adopted therefore oblique incisions carried from the fascia lumborum medial and ventral to the edge of the rectus The external oblique and in part the transversalis muscle are separated between fibers and the internal oblique divided as required If more room is required, the anterior and (above the linea semilunaris) posterior sheath of the rectus are divided and rectus and deep epigastric vessels retracted medially The lower intercostal nerves are retracted without division The liberated loop of colon with adjacent peritoneum, mesentery and lymphatics, is finally exteriorized through the lateral angle of the incision where it lies close to the abdominal wall

For resection of the transverse colon or sigmoid a vertical transrectus incision serves well After exteriorizing the cancerous loop and liberated adjacent mesentery, lymphatics and peritoneum, the opposed antimesenteric arms of the loop are united with fine interrupted sutures of silk and the rest of the wound closed with buried interrupted sutures of alloy (rustless) steel wire Dressings having been applied, the loop of bowel with attached tissue is cut away and bulbous angled glass tubes tied in the two open ends of bowel From the glass tubes soft rubber Penrose drains lead the intestinal discharges into rubber gloves attached to the dressing In five to seven days the glass tubes which lie outside the abdominal wall slough out All dressings are then removed and the abdomen, frequently cleansed, dried and dredged with zinc stearate powder, is exposed to an incandescent light under a bed cage By the seventh to the twelfth day the spur may be divided Without anesthetic, as the bowel is insensitive, the redundant and sloughing ends of the bowel are trimmed and then united where apposed with two No 35 gauge sutures of alloy steel wire tied in a surgical knot With traction on the two sutures the spur is divided for about 1 cm when additional wire sutures to unite the edges and control bleeding are introduced With traction on the two deepest sutures the division and suture are continued until the spur has been divided to a sufficient depth, usually 5 to 7 cm The bowel may then or a few days later be entirely closed with inverting interrupted sutures of No 35 alloy steel wire In this way the spur may be divided and the openings permanently closed in some cases as early as the twelfth day Usually, however, after a lapse of a number of days, additional sutures are necessary with an incision to free the

loops to the depth of the aponeurosis In any case the skin and fascia should not at this early date be sutured for fear of starting a spreading pyoderma of the abdominal wall. The united bowel tends to retract within the wound and

retracting into the pelvis unless it is securely held outside the wound by a strong clamp or other device.

For the adequate removal of most cancers of the proctosigmoid and rectum, a combined one-stage abdomino-

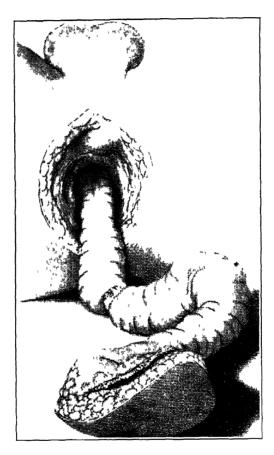


Fig. 18—Removal of pelvic floor with liberated rectosigmoid for carcinoma of the anorectal region. The rectum and sigmoid have been liberated through an abdominal incision, the inferior mesenteric and middle hemorrhoidal vessels having been ligated and divided, and a gauze tape for traction tied about the sigmoid and packed against the pelvic floor. The abdominal incision having been closed and the anus packed with iodine gauze and closed with a purse-string suture, the infiltrated pelvic floor is excised wide of the carcinoma and withdrawn with attached rectosigmoid and pelvic lymphatic tissues. It is important that well vascularized sigmoid be brought to the perineum. The perineal opening is partly closed with buried alloy steel wire sutures, dressings applied, the bowel cut away and a rectal tube tied in the protruding end of the sigmoid. (Courtesy, Southern Surgeon, Aug., 1937.)

spontaneous healing by granulation commonly follows Occasionally a carcinoma of the rectosigmoid may, after liberation to the floor of the pelvis, be delivered through the abdominal wound for an adequate excision by this method There is, however, a danger of the distal end

perineal operation with a perineal anus has a number of advantages. Nearly all patients desire the convenience of a perineal opening. If the opening is of adequate size and care is taken to empty the colon every two to four days, soiling is largely obviated and even the absence

of a sphincter ani is not such a serious matter. The discredit attached to the perineal anus has resulted from the necrosis and cicatricial stricture formation that so commonly follows the Kraske and other forms of perineal proctectomy With viable bowel brought to the perineum which in most cases necessitates proper liberation of the up-

It is also very important that in the liberation or delivery of the bowel cancerous or infected tissue be not entered.

For a carcinoma of the rectum and rectosigmoid, the superior mesenteric or the superior hemorrhoidal vessels are doubly ligated and divided; and with attached fat, lymphatic tissue and peritoneum and sigmoid and rectum are

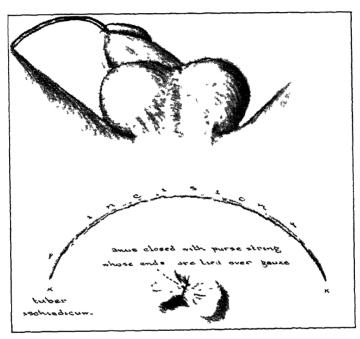


Fig 19—Incision for delivery of carcinoma of the rectum invading the prostate. The rectosigmoid with attached lymphatics has been liberated through an abdominal incision to a point well above the level of the cancer, a gauze tape tied around the sigmoid and the abdominal incision closed. The perineal incision exposes the infiltrated prostate which is excised en masse with the liberated rectosigmoid. The loop of diseased bowel and attached soft structure is cut away between clamps and the end of the sigmoid brought out through the freely split anus. The wound is then closed with superficial and deep sutures and a rectal tube tied in the protruding end of the sigmoid (Courtes). Southern Surgeon, Aug., 1937.)

per sigmoid through an abdominal incision, an adequate anal opening may be formed. The abdominal incision also enables the exploration of the peritoneal cavity for metastasis and the more thorough removal of lymphatics and other involved tissues. If the cancerous segment is retained in the pelvis between stages, necrosis and bacterial permeation may lead to a dangerous form of sepsis before or during the later state

freely liberated to the floor of the pelvis A soft tape of folded gauze one meter long is tied around the sigmoid well above the growth and the ends packed against the floor of the pelvis, and the abdomen completely closed. With the anus closed by suture and covered, an incision is then made through the permeum from just behind the anus to the side of the coccyx, the gauze grasped and the liberated loop of bowel carefully

eased through. After applying dressings the exteriorized bowel is cut away and a rectal tube tied in the ends of the protruding bowel. A week or ten days later the two intervening partitions are slit through into the anus and the margins united with fine alloy wire sutures. After three or four months a very fair degree of fecal control is obtained, especially

diseased tissue which may include part of the prostate or the posterior vaginal wall. The operation is completed by pulling the end of the sigmoid through the dilated and split anal opening and the closure of the perineal incision

For advanced ineradicable carcinoma, Babcock finds colostomy rarely desirable. By restricting the patient to a non-

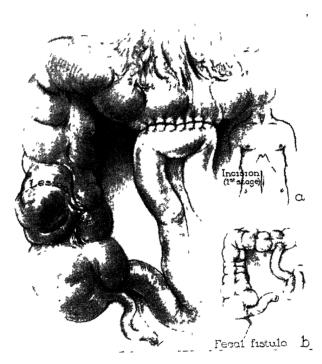


Fig 20—First stage in resection of right half of colon, showing the usual side-to-side ileocolostomy a, Incision b, end-to-side ileocolostomy (preterable in certain cases) (Courtesy, Surg, tivnec and Obst., July 1937)

it the lower bowel is kept empty by using a small enema every 24 to 72 hours. A secondary plastic operation to improve sphincter control is therefore rarely necessary. If the lower rectum is involved by the carcinoma, the pelvic floor is removed together with the anus and attached liberated bowel and a permeal anus formed of the sigmoid. If the prostate or other anterior structures have been invaded a curved transverse incision in front of the anus may be used for the liberation and delivery of

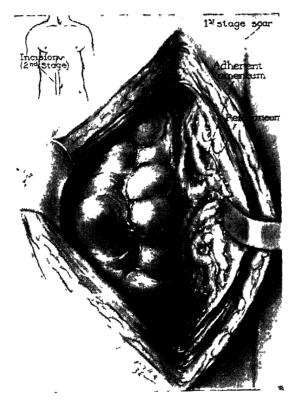
residue diet, by avoiding drastic cathartics, by the use of mineral oil, enemas and a resort to duodenal and rectal siphonage if obstruction develops, the necessity for the operation may usually be avoided. For the patient who is completely obstructed and at the most has only a few weeks to live it is, as a rule, better to let him die obstructed than to render him more repulsive and a greater burden to himself and friends through a colostomy. In the earlier stages when small irremovable metastases are present

in the liver or lymphatics, the radical removal of the diseased bowel without colostomy is often a preferable operation. Several of the patients with hepatic involvement have lived from one to three years in relative comfort after removal of the primary tumor.

J deJ Pemberton and L D Whittaker 15 point out that within recent years

the employment of balanced anesthesia to insure relaxation without noxious effects of deep narcosis, (5) improvement in operative technic, and (6) the more general utilization of the principle of the multiple stage operation

In spite of these advances, however, there are many pressing problems still



lig 21—Second stage in resection of right half of colon, showing omentum adherent to so it of first stage incision. (Courtesy, Surg., Gynec. and Obst., July, 1937.)

there have been many advances in the surgical treatment of diseases of the colon. Of the noteworthy factors which have contributed to its progress, the following may be mentioned. (1) Earlier recognition and treatment of colonic diseases made possible because of improved diagnostic methods. (2) preoperative measures directed to rehabilitation of the patient and to decompression and cleansing of the colon, (3) intraperitoneal vaccination to fortify the patient's re-

confronting the surgeon and these must be solved before surgery of the colon can be considered on a plan equal to that of general abdominal surgery. In support of this it is necessary only to call attention to the high mortality following surgery of the right half of the colon as reported from various hospitals—15 to 30 per cent. When it is realized that among the most frequent causes of failure in colonic surgery are spread of infection (fortiontis) and in-

testinal obstruction, and since these are not always necessarily unavoidable complications, it is clear that there is at least a hopeful approach to the problem.

The employment of the two-stage operation for resection of the right half of the colon and the application of the principles and technic described have combined to give a lower mortality in surgery of the right half of the colon Resection of the right half of the colon as the second stage is the more formidable procedure, but it has been performed at no greater risk and with less reaction than the preliminary stage of ileocolostomy

Secondary resections in recurring carcinoma of the colon are discussed by J W Thompson ³⁶ The author states that in about 50 per cent of cases,

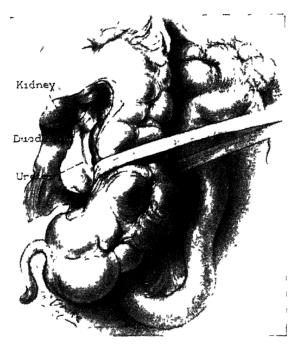


Fig 22—Second stage in resection of right half of colon—Separation of lateral peritoneal reflexion to the right half of colon, showing retroperitoneal structures to be avoided—(Courtes), Surg., Gynec and Obst., July, 1937.)

and at the same time have undoubtedly increased the limits of operability

In a consecutive series of 38 cases second stage resections of the right half of the colon were performed, with two deaths, or a mortality of 52 per cent Ileocolostomy, as a first stage procedure, was performed in 43 cases, with two deaths. These four deaths in the series of 43 cases studied give a total mortality for both stages of 93 per cent. There were no deaths secondary to peritonitis.

beyond surgical relief by the time the patient is first seen by the surgeon. The operative mortality varies from 5 to 35 per cent. Metastasis to the liver and regional lymphatic glands is a specter always haunting the patient surviving operation. The problem of persuading the patient to submit to an operation for recurrence is even more difficult than gaining his consent to the primary operation. Thompson reports a small series

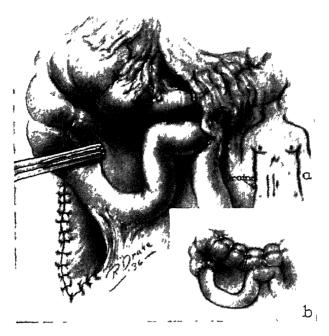


Fig 23—Second stage in resection of right half of colon, showing completion of resection and beginning of end-to-end anastomosis of ileum to colon a, Positions of incisions and stab drain, b, completion of end-to-end anastomosis (Courtesy, Surg, Gynec and Obst, July, 1937)

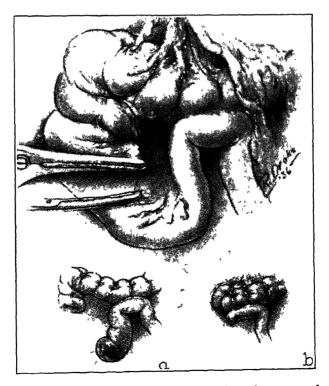


Fig 24—Second stage in resection of right half of colon, showing marked disproportion between end of ileum and end of colon, preventing accurate end-to-end anastomosis a, Incorrect closure of ileum, giving rise to distended loop with possible perforation, b, correct closure of distal ileum close to site of ileocolostomy (Courtes), Surg, Gynec and Obst, July, 1937)

of cases in which a second resection of the large bowel was performed for recurrence successfully While the recurrence of many malignant growths is often prompt, in some cases many years elapse between the primary operation and the recurrence Ewing has reported a case of breast malignancy in which the interval was 30 years, a case of rectal cancer in which it was 21 years, and a case of uterine carcinoma in which it was 15 years There is always the possibility that the defenses offered by immunity may isolate and destroy remaining cells or surround them by dense connective tissue

Thompson reports three cases in which recovery took place following resections for recurring carcinoma of the colon. The interval between operations in the first case was three years, in the second case 12 years and in the third case nine years.

The author concludes that recurring caremoma of the colon is not always a hopeless lesion. Multiple malignant lesions of the colon are probably not so rare as is commonly believed. They may occur simultaneously or develop after a period of many years of intervening good health.

Diverticulitis of Colon

Many cases of colon disturbance are labeled and treated as "colitis" without proper examination and study R R Graham ¹⁷ states that most of such cases are functional but occasionally there is an organic lesion responsible especially carcinoma or diverticulitis. The reason for seeking relief is one of both of the following reasons a change in the rate of flow of the content (diarrhea or constipation) or a change in character of the content (increase or decrease of fluid, presence of blood, mucus, or pus)

Diverticulosis which must precede diverticulitis, is present without symptoms in about five per cent of persons subjected to x-ray examination of the colon for any cause Diverticulitis develops in approximately 12 per cent to 15 per cent of cases of diverticulosis. The frequency of diverticulosis is about 12 in a thousand, that of diverticulitis is one in a thousand Diverticulitis rarely occurs under 35 years of age. This study of 44 cases covers a group which had progressed to a point requiring surgical consultation.

Acute diverticulitis is divided into single, nonperforating, and perforating, and perforated Chronic diverticulitis is divided into nonperforating with adhesions and obstruction and slowly perforating with abscess about the sigmoid, in the mesentery, or into adjacent viscera Twenty-five per cent of the patients in this study underwent emergency operation for acute perforation Diagnosis in the acute group is difficult. No mass was palpable in the acute cases "Pain in the lower abdomen—radiating to the rectum and temporarily relieved by the passage of flatus or stool, is a very significant symptom" The results from general treatment with intravenous fluids. heat locally, and sedation are justified even though operation is delayed several hours Operation consists of exposure of the perforation, the placing of a rubber tube to the site, and walling off the surrounding area with gauze saturated with liquid pariffin containing BIPP In obstruction requiring decompression a cecostomy is preferred to a colostomy because it is simple, effective, easy to close, and it acts as a safety valve if resection is necessary Cecostomy is done by attaching the bowel to the skin by interrupted sutures

Most cases of chronic diverticulitis are characterized by "recurring vague abdominal distress with definite periods of acute illness" in patients over 40 years of age Symptoms commonly consist of constipation, fever, and acute pain Less often there is bleeding, tenesmus, obstruction, lower abdominal mass or a tender mass palpable rectally X-ray is of distinct help in many but not all cases The cases treated were practically all surgical and therefore an opinion concerning early treatment is of no value Based on the few nonsurgical cases, however, treatment would include prolonged bed rest and dietetic control with periodic examination over a year or two provided response is satisfactory Resection in the cases not responding to the above treatment would save invalidism, economic loss of time, and the possibility of erroneous diagnosis especially in carcinoma of which there were seven cases in this group

The presence of a mass is not an indication for emergency treatment. Nor should a patient with a left colon mass be diagnosed carcinoma until diverticulitis has been excluded etiologically. There were 13 diagnostic errors in this group of 44. Five cases diagnosed diverticulitis proved to be carcinoma. Differentiation of inflammatory and neoplastic lesions of the colon may be very difficult or impossible or the two may coexist.

Seven thousand consecutive autopsies were studied by E. J. Kocour. With regard to the incidence of diverticulosis. Of the cases over 40 years of age 3.58 per cent showed diverticulosis and 0.15 per cent showed some complication which had caused the death of the patient. After 40 years of age, the incidence in the white male and colored female is approximately the same, while in the white female the incidence is over one-third again as much, in the colored male it occurs only two-thirds as often

There were only two-thirds as many colored persons with diverticula as white persons. Most of the diverticula were found in the sigmoid colon and in the sigmoid and other regions of the colon; all those which had produced complications were situated in the sigmoid colon.

The incidence of carcinoma of the colon, essential hypertension or peptic ulcer was not greater in the group of patients with diverticulosis of the colon than in the entire group studied. However, the incidence of lesions of the gall bladder in patients over 40 years of age was doubled in those with diverticula. No explanation for this is offered at the present time, but it bears out the clinical impression that a relation exists between abnormal colon function and cholecystopathy.

Polyposis of Colon

The method of treatment of disseniinated polyposis of the colon which C W Mayo and E G Wakefield39 describe seems to have qualifications which still further advance the care of selected patients who have multiple polyposis of The normal outlet of the the colon rectum and its sphincters is preserved, and the rectosigmoid and sigmoid flexure, which contain the nervous mechanism controlling the desire to defecate, are left intact Therefore sufficient room is left for the storage of fecal material Primarily, the operation has been made possible by the development of improved instruments and improved technic on the part of proctologists Mayo and Wakefield were assisted by Buie and his colleagues in the Section on Proctology at the Mayo Clinic, who removed the polyps from the rectum, rectosigmoid, and sigmoid in order that segments which were free of polyps might be utilized in performing an ileosigmoidostomy

The first stage of the operation is performed by the proctologist, who, with repeated applications of diathermy, removes a few polyps at a time as conditions permit until the rectum and rectosigmoid are free from polyps second stage of the operation is not performed until the rectum and rectosigmoid are free from polyps and the inflammation incidental to their removal This stage of the procedure, which is performed through a right rectus incision, consists of end-to-side ileosigmoidostomy and hemicolectomy with removal of the right half of the colon and of as much of the transverse colon as can be removed with ease. In the performance of the ileosigmoidostomy care is taken to cut the ileum at an angle that insures not only a large stoma but also a good blood supply to the incised edge anastomosis is made along the longitudinal band with a serous layer of silk sutures and mucosal layers of sutures of chromic catgut. The angles of the anastomosis are protected with extra interrupted sutures of silk, which include epiploic tags whenever possible incised end of the remaining portion of the transverse colon, with a Pavr clamp closing it, is brought out of the upper part of the right rectus incision after intra-abdominal raw surfaces have been covered with peritoneum. A rectal tube is fixed in the rectum to allow free passage of liquid and gas

The third stage, which is carried out as soon as conditions permit, consists of hemicolectomy again, this time performed through a left rectus incision with removal of the remaining portion of the transverse colon, the splenic flexure, and the descending colon. The amount of colon to be resected may be judged by palpation of the polyps. As the proximal portion of colon is brought out of the wound, which makes it possi-

ble to fulgurate when necessary through the colonic stoma at a later date, it may be possible to save more of the colon than has been reached from below with the sigmoidoscope. In performing resection of the transverse colon it is important to preserve as much of the omentum and its blood supply as possible

The fourth stage of the operation consists of retrograde examination and fulguration through the abdominal colonic stoma

The fifth step is closure of the colonic stoma, which re-establishes the continuity of the intestine

Strangely, little if any fecal drainage occurs through this colonic stoma at any time before closure. It may be left as a safety valve for a while and closed later, after repeated examination has revealed that the remaining portion of bowel is free from polyps

With regard to the type of case to which this procedure is applicable the authors state that it cannot be used when secondary inflammation has involved the entire colon. This condition is best treated by ileostomy and total colectomy in stages after the inflammation has subsided. The surgical treatment described is of particular value in cases in which the diagnosis is made before complications have developed, particularly when carcinoma has not involved the colon distal to the sigmoid flexure.

As soon as multiple polyposis of the colon is diagnosed and the described method of treatment is considered applicable, the first stage of the operation should be started. While this is admittedly a formidable surgical procedure, it is the only known way of guarding the patient against repeated intestinal hemorrhages and carcinoma. In most cases, instead of being a prophylactic measure, the operation removes degenerated



Fig 25—A large, massive irregular filling defect is shown at A, involving the ascending colon, presenting all the characteristic roentgen signs of a carcinomatous growth. Note the irregular tract at B leading towards the spinal column. (Courtesv. Am. J. Digest. Dis. and Nutritional. April 1937.)

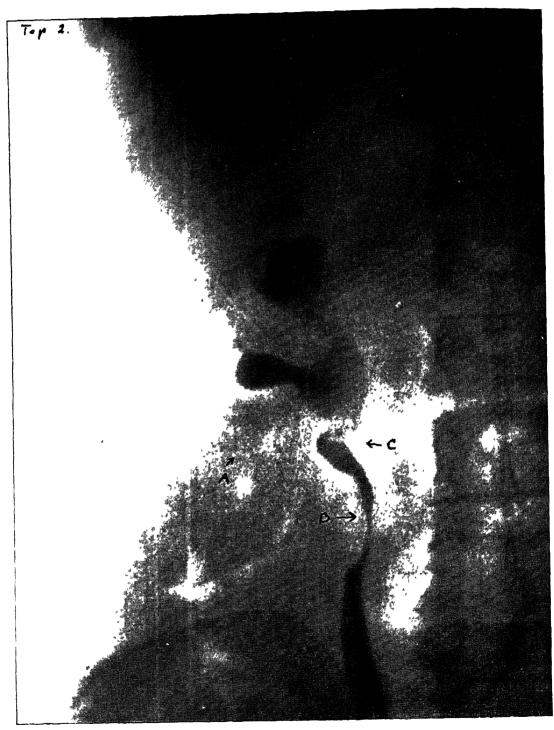


Fig. 26—Retrograde pvelogram illustrates the poor filling of the kidney pelvis and faint outline of the inferior cally at 4. The superior cally is dilated and blunted. Note the pressure defect upon the upper ureter at B produced by the mass. A ureteral kink is shown at C. (Courtesy Am. J. Digest. Dis and Nutrition, April 1937.)

polyps and multiple carcinomas which are already present.

Of 19 patients under 41 years of age, 12 were women and seven were men The hereditary and familial tendencies. if present, do not admit any known genetic or biologic interpretation. In six of the patients a carcinoma was the predominating lesion at the time of operation It has been said that the development of carcinoma in these colons is inevitable, that uncomplicated polyposis of the colon is symptomless, and that diarrhea and blood in the stools are not signs of polyposis but evidence of serious complications such as secondary infection, ulceration, or carcinoma An ulcerative colitis may develop on an existing polyposis of the colon with subsequent disappearance of the polyps The described new surgical procedure is designed to reduce the operative risk, conserve the distal segment of the colon and the entire rectum, and eliminate the necessity for permanent ileostomy

Renocolic Fistula

A renocolic fistula is described by M Feldman40 which is the second case of this type described. In this presentation a renocolic fistula is recorded in which the barium enema gave the first clue as to the true nature of the condition The barium enema revealed a large irregular filling defect in the ascending colon presenting all the characteristic roentgen signs of a malignant growth with a large mass on the right side On close observation, an irregular narrow channel could be seen leading from the colon toward the mass which suggested a fistulous tract A pyelographic study was also made in this case, which presented evidence of a pyelonephritis The fistulous tract is not visualized on the pyelogram, which indicated that the communication existed between the colon and perinephritic abscesses of the right kidney. A fistulous communication was observed between the kidney mass and the ascending colon

The roentgen ray offers the only means of establishing a preoperative diagnosis

Ulcerative Colitis

The various names given to inflammations of the colon, colitis gravis and ulcerosa, and suppurative colitis, always mention only one predominant characteristic of the disease O Odén⁴¹ points out that gradually a typical, independent clinical picture is formed which stands out from the ordinary mucosal or mucomembranous inflammations of the colon and is characterized by a more marked inflammatory reaction of the mucous membrane and the occurrence of ulcers The ulceration varies from a few small ulcers to extensive, closely packed ulcers. more or less deep, which involve almost the entire mucous surface Severe diarrhea with mucus and blood alternates with periods of obstinate constipation

This form of colon inflammation was first described as a rare condition by the Englishman, Wilms, in 1875 After the World War a series of from 500 to 600 cases was reported in America Boas introduced the name "ulcerative colitis" in 1902 The English and French (Mathieu, Lockhardt-Mummery) proposed the term "colitis hemorrhagica" for the more hemorrhagic forms names in the literature of the investigators of this condition are numerous. and the causes which have been attributed to the condition are equally numerous Ulcerative colitis is believed to be the sequel to dysentery (Pels Leusden, Ehrmann), focal infection in the tonsil or periapical abscesses (American reporters), prolonged constipation and resultant damage to the

mucosa, functional disturbances, avitaminosis, anaphylactic states, hemorrhagic diatheses, and many more conditions. In any event, all other causes (lues, tuberculosis, amebiasis, sinusitis) must be excluded before the term ulcerative colitis may be applied

In general, the age of the patients ranges between 20 and 40 years, and women are affected more often than men Minute description of the pathologicoanatomical changes is unnecessary because they are so well known. The course and symptoms vary from the most acute onset and rapid death, or gradual subsidence and recovery, to insidious onsets with gradual transformation to subacute or chronic states The clinical findings vary accordingly Blood-sedimentation determinations may reveal values as high as 100 mm per hour The blood picture shows a shift to the left in most cases. Stool examinations show no constant findings. The proctoscopic picture is most characteristic, but carcmoma must be ruled out Roentgen-ray examination is of decisive value except in the mild cases. On the basis of Weber's roentgenological studies and results, which the author recognizes as being very valuable, it may be assumed that the roentgen diagnosis of colitis is well known. There are numerous complications. Secondary anemia peritoritis, premie pulmonary metastases, and others. The prognosis is correspondingly variable, but usually very grave because of the tendency toward chronicity and recurrence

Numerous treatments are advocated They fall into two groups surgical and nonsurgical. The latter includes dietetic and hygienic measures, drug therapy, bowel irrigations, vaccine or serum treatment, blood transfusion, and injection of metallicsalt (manganese) Surgical treatment was recommended as

early as 1885 by the French writer, Folet, who advised *cecostomy*. When operative treatment was limited to palliative measures, such as *appendicostomy*, colostomy, or ileosigmoidostomy, it was not entirely satisfactory. Therefore, surgical treatment became more radical (Lane, Nordmann, Rotter, Jordan, Kiefer, Dahl). The results were relatively good, with cures in 50 per cent and improvement in 25 per cent of the cases (Leischner), but the mortality was about 15 per cent

In this paper four cases are reported in detail with temperature curves and roentgenograms. In these cases medical treatment and cecostomy were without effect and colostomy was considered

Regional Colitis-According to A Hurst and F A Knott42 regional colitis may be regarded as a form of ulcerative colitis in which the disease is localized to a single segment of the colon The rectum and lower part of the pelvic colon are not involved. It was first described as a clinical entity by Bargen and Weber in 1930 and so far as the author is aware, no other article has appeared in the literature on this particular subject Bargen and Weber described 11 cases, in which there was no sigmoidoscopic evidence of ulcerative colitis, although the patients had characteristic symptoms, an opaque enema showed that ulcerative colitis was present in an isolated segment of the proximal colon The diagnosis was confirmed by laparotomy in 11 patients and by autopsy in three patients

A case of regional ulcerative colitis associated with bacillus asiaticus was cured by partial colectomy. A medical man, age 41 years, had had bilateral pulmonary tuberculosis at the age of 20 years. He recovered and was able to take care of a large general practice. In February, 1935, he felt very tired and

had an attack of colic and diarrhea with the passage of blood in the bowel movements. This condition persisted for three months Severe colicky pains recurred in the left side of the abdomen and the bowel movements were attended with great pain A carcinoma of the colon was suspected but sigmoidoscopy was negative By September, 1936, he was passing six stools per day There was much blood present Abdominal pain was severe in the left lower abdomen He vomited when forced to eat solid foods The descending and iliac colon could he felt as a hard cord The blood count was nearly normal and he had no fever. An opaque meal revealed a normal colon as far as the splenic flexure where there appeared to be a considerable degree of obstruction, the result of spasm The typical appearance of severe polypoid ulcerative colitis was clearly visible in the entire descending and iliac colon In addition to the usual bacillus coli communis and the enterococcus, the stools contained large numbers of a nonlactose fermenter, which proved to be bacillus asiaticus It was agglutinated by the patient's serum in a dilution of one to 50 No tubercle bacıllı could be found on repeated examination

A diagnosis of regional colitis was made and laparotomy performed. Jones removed the colon from a point in the transverse colon 5 in (127 cm) from the splenic flexure to a point in the pelvic colon 3 in (76 cm) from the junction with the iliac colon. An end-to-end anastomosis was made together with a temporary eccostomy. Recovery was uneventful and by October the patient was feeling very well. His stools were normal and no occult blood was present. Repeated cultivations of the stools showed the absence of bacillus asiaticus.

Microscopic examination of the excised portion of the colon showed a severe inflammation, but no evidence of tuberculosis. Some polyps were present which were true adenomas, but others were pseudopolyps or tags of simple hypertrophic mucous membrane separated from the intestinal wall by the ulcerative process At the base of these tags, ulceration persisted in some areas, in others healing had taken place

Colectomy or Colonic Exclusion with Ileostomy in the Treatment of Ulcerative Colitis and Polyposis-L. D Whittaker and J A Bargen⁴³ have studied both the immediate and late effects of total colectomy or colonic exclusion on 45 patients Colectomy or colonic exclusion by ileostomy was done only after conservative treatment had failed The three most frequent indications were refractory chronic ulcerative colitis, chronic ulcerative colitis with polyposis, stricture or perirectal abscess and hereditary polyposis. The values for the serum calcium were slightly reduced following colectomy or ileostomy but returned to normal within a month Colectomy or ileostomy does not otherwise disturb the physiologic equilibrium of the chemical constituents of the blood Roentgenologic visualization or the appearance of the terminal portion of the ıleum at operation or necropsy revealed a definite dilatation There was no evidence that the dilatation was sufficient to compensate volumetrically for the excluded colonic reservoir Stools from the ileac stomas were alkaline. The average weight of the stools while the patients were on a general diet was 433 Gm and the water content was 912 per cent The watery discharge gradually thickened during the first three months This thickening of the stool is unrelated to the time necessary for the ingested material to be expelled from the ileac stoma

There was no fundamental change in motor activity or in the intestinal response to the ingested food throughout the prolonged period following operation A period of three months is necessary for the patients to regain their average weight and strength No permanent deficiencies in metabolism follow ileostomy

Technic Colon Surgery—Closure of Colostomy—In the experience of F W. Rankin and A S Graham⁴⁴ more than one-half of the cases in which obstructive or exteriorization type of colon resection was done the colostomy closed spontaneously after a period of from six weeks to two months Failure of the colostomy to close may be due to spur formation, attachment of the mucosa to the skin edges, or to obstruction beyond the colostomy

The preparation of the patient for insertion of clamps should be as elaborate as that for the primary resection. The author uses long curved Kelly forceps which are inserted and closed to the first notch. Each subsequent day the clamps are tightened one notch. Usually the septum is cut through in five to six days, but occasionally a forcep will hang on for eight to nine days. It should never be pulled out—they should be allowed to fall out.

In closing the colostomy an elliptical incision is made through the skin, around the stoma down to the fascia. The index and middle fingers are now inserted into the two ends of the bowel, using them as retractors. The dissection is now carried down to the peritoneum on all sides. The margin of skin which has been left on the ends of the bowel are cut away and the stoma closed with two rows of chromic catgut sutures placed transversely. A third row of sutures may be used if there is ample room, or it seems necessary. Any disparity between the

size of the two segments of bowel may be overcome by splitting the wall of the smaller one After flushing out the wound with saline and later ether, the fascia is closed by interrupted sutures. The skin edges are loosely approximated and rubber tissue drains are inserted down to the fascia. The percentage of closure by primary union is remarkably high

DUODENUM

Diverticula of the Duodenum

In spite of the relative frequency of duodenal diverticula, the clinical manifestations and treatment have by no means been well established According to J Mialaret⁴⁵ very often certain symptoms have been attributed to the presence of a diverticulum when they could have been explained by some associated lesion Various methods of treatment have been employed without precise indications, and little is known of the late results of operative procedures

Etiology—Eighty-five per cent of duodenal diverticula occur in the second portion of the duodenum, nearly all arise from the concave surface and are more or less intimately connected with the pancreas Occasionally they are multiple or associated with diverticula elsewhere in the intestinal tract. Most of them are the false type, consisting of a hernia of the intestinal mucosa along the blood vessels. They seldom occur in a patient less than 50 years old.

Symptoms—On the basis of the symptomatology, six types can be recognized

1 The dyspeptic type The patient complains of discomfort and pressure in the epigastric region which occurs a variable time after eating and lasts for a variable period. These symptoms occur in the absence of inflammatory changes

and are due to simple distension of the diverticulum

- 2 The pseudo-ulcerous type This is the most common type and is due to diverticulitis
- 3 The pyloric stenosis type The symptoms result from compression of the duodenum by the distended diverticulum
- 4. The intestinal type Vague symptoms of enteritis are noted
- 5 The gall bladder type In this type there are crises of pain in the right hypochondrium which closely simulate gallstone colic Also, there may be icterus
- 6 The pancreatic type Intense periumbilical pain which occurs without relation to meals, vomiting, diarrhea, loss of weight, and sometimes icterus are noted If the latter condition is present the symptoms may simulate those of a pancreatic tumor

The complications to which diverticula are occasionally subject include acute inflammation, perforation, gangrene and rarely cancer

Diverticula are seldom responsible for digestive symptoms Demole in 1936 stated that in 46 cases of diverticula observed roentgenologically, some other associated lesion was responsible for the symptoms Considering only the cases confirmed at operation, hardly a dozen could be found in which the diverticulum appeared to be the essential trouble. The case histories of four such cases are In three patients there given briefly had been prolonged postprandial distress with vomiting, the fourth suffered from profuse gastric hemorrhages In each case removal of the diverticulum was followed by permanent relief Similarly, case histories are cited in which diverticula were the cause of biliary and pancreatic symptoms

Treatment—Operative treatment has given an immediate mortality of about 16 per cent. This includes cases in which other lesions, such as cholelithiasis, were treated at the same time. As far as diverticula alone are concerned, the intrapancreatic diverticula offer the greatest operative difficulties and dangers.

Because operative treatment carries real risks and a diverticulum is seldom a menace to the life of a patient, it may be asked to what extent an operation is justified by its late results. In 22 unpublished cases collected by the author the results were as follows: an error in diagnosis was made in two cases, postoperative death occurred in one, and complete cure was obtained in three

Indications for operation can be considered only after a complete study of the patient. This study should not merely establish the existence of the diverticulum, but should make certain that no other lesions are present. If the diverticulum is the only lesion that can be detected, operation may be done because of progressive loss of weight, rebellious gastrointestinal symptoms or interus. Even under these circumstances the intervention will be in the nature of an exploratory operation with the diverticulum as a secondary consideration.

Among the operations that have been employed *resection* of the *diverticulum* is the best. When icterus due to the diverticulum and changes in the pancieas is present, *drainage* of the biliary tract should follow the resection.

Duodenal Obstruction

The obstetrician and pediatrician should regard vomiting of the newborn infant as a symptom demanding investigation of the alimentary tract. Many infants may thus be given a chance for life which was formerly denied them

TABLE 3
SUMMARY OF THE FINDINGS IN THE SEVEN CASES OF DUODENAL INTUSSUSCEPTION

| Case | Age | Sex | Symptoms and Signs | | | | Laboratory Findings | | | | | Pathological Report | | |
|------|-----|-----|--------------------|----------|------|----------|------------------------|-------|--------|----------------|-------------------------------|------------------------|-----------|-----------------------------|
| | | | Duration | Vomiting | Paın | Weakness | Weight Loss | Tumor | Anemia | Blood in Stool | X-ray | Treat- ment | Outcome | |
| 1 | 47 | M | 6 mos | + | + | + | | | | | | Medical | Died | Constricted duodenum |
| 2 | 25 | М | 10 mos | + | + | + | | | | | | Medical | Died | Fibro muscu- lar polypus |
| 3 | 21 | М | 12 mos | + | + | | | + | | | | Surgical | Died | Polypı |
| 4 | 75 | F | | | | | | | | | | | Cadaver | Fibro- adenoma |
| 5 | 69 | М | 4 mos | + | 0 | + | + | | + | + | of duo- | Surgical | Recovered | Benign adenoma |
| 6 | 58 | М | 12 mos | + | + | + | | 0 | | + | denum and upper jejunum | Medical | Dıed | Mucus adenoma |
| 7 | 62 | F | 9 mos | + | 0 | + | + | + | + | + | Dilated duodenum | Surgical | Recovered | Papılloma |

⁽Courtesy, Am J Digest Dis and Nutrition, July, 1937)

W E Ladd⁴⁶ points out that posterior duodenojejunostomy is the operation which has proved most successful in relieving intrinsic duodenal obstruction. Of the other types of operations used the one that seems most logical is the plastic operation on the duodenum described by Morton.

For the extrinsic type of duodenal obstruction the transposing operation described by the author is the one of choice. The reduction of the volvulus alone is not sufficient to relieve permanently the obstruction of the duodenum due to malrotation of the midgut.

J L McGehee and W D Anderson⁴⁷ report a case of *chronic obstruction* and *dilatation* of the *duodenum* in a female 18 years of age At the operation they found that the duodenum was distended to the part crossed by the superior mesenteric artery. They re-

lieved the obstruction by a duodenojejunostomy

Duodenal Intussusception

According to W W Boardman and E Leivers, 48 duodenal intussusception occurs so infrequently that it is seldom mentioned. Kellogg reports 11 cases gathered from the literature during the past hundred years. Of these, five originated in the stomach, thus leaving only six of true duodenal intussusception. The authors review the so far six reported cases and add one additional case.

In Table 3, the authors have tabulated the essential findings in these cases From this review, it is evident that duodenal intussusception occurs in both males and females in an age ranging from 21 to 75 years. Symptoms were present from four to 12 months before being relieved by surgery or terminating

in death. The outstanding symptom has been vomiting, occurring irregularly after meals and starting usually intermittently but becoming more frequent and more severe. Pain may or may not be present. Weakness and loss of weight are marked. Physical signs other than emaciation may be absent but the finding of a tumor in the upper abdomen, especially if it is inconstant in appearance and variable in size and shape, should make one suspect intussusception

Of the laboratory findings, occult blood in the stools and anemia are apparently constant

X-ray examination has so far proven disappointing primarily because the significance of the finding was not appreciated. In Kellogg's case, the barium shadow of the dilated duodenum is interrupted by a spherical mass surrounded by a ring of barium which as Kellogg reports was described by Carmen as typical of tumor formation but which was interpreted in this case as obstruction due to adhesions

In Case VII, there was abrupt termination of the barium shadow of the markedly distended loop of duodenum and yet the x-ray department reported that no pathology could be demonstrated. In their subsequent report the fact that the obstruction was inconstant made diagnosis difficult for the possibility of intussusception was not considered.

In all but one of these cases a benign tumor was the exciting factor in the development of the intussusception. Tumor of the bowel is recognized as one of the primary etiological factors in the production of intussusception in adults. Benign tumors of the duodenum account for only about five per cent of the benign tumors of the bowel. Frequently, no symptoms are produced but as reported by Balfour and Henderson in a study of 14 cases, benign tumors of the duo-

denum may be responsible for serious symptoms, particularly hemorrhage. Raiford, in a report of 48 benigh tumors of the small intestine found ten in the duodenum. He states that "invagination seldom occurs and symptoms when present are brought on by encroachment of the tumor mass upon the lumen, giving rise to slowly developing obstruction."

It would thus seem difficult to differentiate the symptoms arising from primary tumor with obstruction from those arising from tumor complicated by intussusception, except that the symptoms of obstruction from tumor would probably be more constant than those from intussusception. An evanescent mass is probably the most typical finding

Treatment — Treatment is obviously surgical and should be successful if complications are not encountered. Naturally, the earlier the diagnosis is established and treatment undertaken, the better the prognosis. The postoperative course in the Stanford case was extremely difficult because of the deficiency states.

The conclusions are that true duodenal intussusception does occur but is a rare lesion

It is usually secondary to a benign tumor of the duodenum

It may occur in males or females and from 21 to 75 years

Vomiting, emaciation, anemia, evanescent epigastric mass, and x-ray evidence of dilatation of the duodenum are the usual findings

Surgical treatment should be successful if complications are not encountered

Carcinoma of Duodenum

A case of primary carcinoma of the duodenum is reported by J O Woods ⁴⁹ He comments that a number of interesting features were present in this case Worthy of note is the extensive pathology present with a paucity of symptoms

This man was able to carry on heavy work with little or no discomfort and to his immediate family seemed in his usual health. The onset of symptoms was very sudden, and death followed in only two days. The precipitating cause of death was gross hemorrhage of marked degree, which is a rather common cause of death in other reported cases of carcinoma of duodenum. Gross appearance of the growth suggested a true colloid cancer, but closer study showed the

in the literature presenting this feature Fairly normal duodenal mucosa was present for a distance of 10 cm between two craters, and the growth had apparently extended principally along the submucosa and muscular layers. In this way the duodenum was short-circuited, but the pancreas did not appear to be involved in the growth. The duodenal contents apparently had passed through the new opening, at least to a partial degree

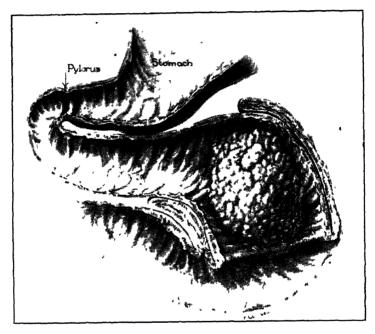


Fig. 7—Cis- VII. Drawing showing the papilloma in the duodenum and the intussusception (Courtes) Am. J. Digest. Dis. and Nutrition. July, 1937.)

colloid-appearing substance to be largely hyalmized tumor detritus. Metastases were not found, which is also remarkable considering the extent of the primary lesion. The origin was apparently from the duodenal mucosa as Brunner's glands appeared normal in microscopic sections.

Perhaps most notable, however, was the spontaneous pathologic duodeno-duodenostomy between two portions of the duodenum. This was produced by extension of the growth, and as far as can be ascertained this is the first case reported In conclusion a case of primary adenocarcinoma of the duodenum of the suprapapillary type has been presented and its unusual features emphasized. The characteristic findings in various types of duodenal carcinoma have been summarized. While this is a relatively rare condition, it is deemed that knowledge of the uncommon lesions should supplement that of the more frequent pathologic findings. It is hoped that a more careful study will disclose more instances of carcinoma of the duodenum and increase the common knowledge of the profession.

Twelve cases of primary carcinoma of the duodenum are reviewed by L M Nissnevitch⁵⁰ who draws the following conclusions

- 1 Primary carcinoma of the duodenum is comparatively rare. It constitutes only two per cent of all cancers of the gastrointestinal tract
- 2 It is most frequent at the usual cancer age. The average age of the patients whose cases are reviewed was 51½ years
- 3 It is more frequent in males than in females Of the patients whose cases are reviewed, 66 per cent were males
- 4 Its origin is usually an old chronic ulcer of the duodenum
- 5 The most common form is the adenocarcinoma. This was the type in 60 per cent of the cases reviewed. Other types are the scirrhous cancer, the collection cancer, and carcinoma simplex.
- 6 It usually forms metastases in the organs and lymphatic nodes of the upper part of the abdomen
- 7 It must be differentiated from secondary involvement of the duodenum by the growth of a carcinoma in the stomach, pancreas, or gall bladder or by metastasis from a carcinoma in an adjoining organ
- 8 Its differentiation from *secondary* cancer of the duodenum is rather difficult not only during life but also at autopsy
- 9 Treatment gives poor results The prognosis is seldom favorable, the period of survival being rather short in all cases

GALL BLADDER

Cholecystitis

Symptoms, Diagnosis, and Management—Next to the diseased appendix, an abnormal biliary tract is the most

common cause of indigestion and abdominal colic In middle-aged women it is the predominant cause Twenty per cent of all women and four per cent of all men eventually have gallstones

According to W W Babcock⁵¹ cholecystitis has been divided into three stages An initial stage of catarrh, a secondary stage of stone formation and colic, and a final stage of late complications Oualitative dyspepsia characterizes the first stage with an idiosyncrasy to certain foods, sour, bitter eructations, gas distention, occasionally a myalgia, neuralgia, arthritis, or myocarditis from the focal infection About 40 per cent of these patients have normal roentgenray findings By the use of duodenalbiliary drainage, epithelial cells from the gall bladder or bile ducts, excess of leukocytes, bacteria, and other changes in the bile may be found to confirm the clinical opinion that cholecystitis is present. Such patients often obtain great relief when given a carefully selected diet with alkalies, mild laxatives, and perhaps the use of a mixed colon or autogenous vaccine ()n the contrary, in about 35 per cent of persons who have no clear history of biliary catarrh or colic, but in whom the gall bladder is considered diseased because it does not visualize on roentgen-ray study, a normal gall bladder will be found at operation, whereas in about four per cent of those in whom gallstones are apparently shown on the film, none are found at operation

In the second stage a stone obstructing the outlet of the gall bladder gives rise to recurrent, acute, severe frequently nocturnal colic, lasting from 20 minutes to two or three hours and termed by the patient "acute indigestion". The attack commonly occurs in a middle-aged obese woman and often follows pregnancy. There is a sense of epigastric pressure and desire to empty the stom-

ach Tenderness under the ensiform may be present, but as a rule there is no tenderness over the gall bladder The condition is to be differentiated from an anginal attack or from coronary occlusion, in which there is dyspnea, a marked fall in blood pressure, and change in cardiac sounds. In about 20 per cent of patients in this stage, the gall bladder will not visualize nor stones be shown by cholecystography and clearcut clinical symptoms alone, dependable in about 94 per cent of these cases, give the most reliable diagnostic evidence of the condition If the clinical picture is blurred, the finding of cholesterol crystals and pigment in the duodenal dramage may best indicate the presence of gallstones Competent internists find this dependable in about 93 per cent of the cases The treatment of cholecystitis in the second stage is cholecvstectomy

In the third stage a frequent complication is the impaction of a stone in the neck of the gall bladder with secondary distention, pressure necrosis of the lining mucosa, and finally a gangrenous and purulent cholecystitis. Ten per cent of the patients admitted to our service for biliary disease and nearly all admitted in colic have this condition. As a rule the diagnosis is easily made from the fact that the colic has lasted more than four hours. Within 24 to 48 hours the enlarging gall bladder may be palpated where it projects below the right costal border Until the parietal peritoneum has been irritated, there is little or no tenderness. The mass, the secondary irritation of the overlying peritoneum with sensitiveness, and muscular rigidity near McBurney's point are responsible for the not uncommon diagnosis of appendiceal abscess This error should not occur if the history and clinical signs are considered A previous history of gall bladder colic is common, and the mass, differing from that of appendicitis extends up under the ribs Cholecystography and duodenal drainage, valueless and harmful during such a severe attack, should not be considered.

The mild local signs, the slight general reaction with low leukocyte count, a temperature of only 100° to 101° F (377° to 383° C), and the slow pulse despite the severe pain encourage delay in the operative treatment of this condition After the first week, colon bacilli and other organisms often invade or multiply in the necrotic walls, and the gall bladder contents develop a high degree of virulence for the peritoneum During the first week a cholecystectomy or cholecystostomy may be done with a mortality of not over four per cent, but after this time the danger of operation rapidly increases until the attack subsides and the simplest form of cholecystostomy has a high mortality Consequently, many surgeons advocate delay in operating until the acute attack is over Doubtless this is much safer than indiscriminate intervention, but it does not eliminate the mortality from perforation of the gall bladder, secondary peritonitis and abscess, internal fistula, intestinal obstruction from gallstones, and the like In 40 cholecystectomies for purulent or gangrenous cholecystitis performed in the first week of the attack there was one death. In 42 cholecy stostomies done later, usually for the more advanced or complicated conditions, the mortality exceeded 20 per cent—a mortality evidently much greater than if delay for subsidence of the attack had not been practiced When the bile was found—at operation—to be fetid or ammoniacal, the mortality from the simplest cholecystostomy exceeded 40 per cent Babcock, therefore, has modified the operative procedure as follows all cases operation is done within 24 hours after admission to the surgical service, or as soon as the patient can be put in operable condition.

During the first week of the attack. if the patient is young or in good general condition and if on exploration there is no evidence that the infection has spread beyond the gall bladder, a cholecystectomy is done without aspiration or spilling of the gall bladder contents In case of any doubt and in all cases in which the patient has had the attack more than seven days or is a poor risk, as from obesity, senility, peritonitis, associated damage to liver or myocardium, the gall bladder is not removed or opened, but the operation is done in two or more stages Through a rather small vertical upper rectus or a muscle-splitting incision, the large distended gall bladder is exposed and, if free, is immediately tilted outward through the incision, where it is held by closing the wound about it without drains If on account of obesity or fixation of the gall bladder the fundus cannot thus be exteriorized, a special large glass tube, 3 to 6 cm in diameter and with a rounded lower edge, is introduced to the side or fundus of the gall bladder, against which it is held by fine alloy steel sutures brought out through the appropriate openings in the glass tube. The wound is then closed about the tube without additional drainage Forty-eight or more hours later a large button is burned out of the wall of the exposed gall bladder with a fine cautery point Some days later gentle attempts are made to remove the contained stones When the tract is narrow, the stone may be exposed through an open cystoscope or urethroscope and, if impacted, softened by applying small cotton swabs saturated with ether to dissolve the cholesterol to permit its fragmentation

Thus far the author has had no mortality in cases in which the described technic

of these exteriorization operations has been carried out. The fact that the patients obtain almost immediate relief after the large glass tube has been introduced against the tense unopened gall bladder seems to indicate that the pain comes chiefly from the peritoneal irritation

Muscle-Splitting Incision — To facilitate the early closure of the wound after exteriorizing the gall bladder Bab-

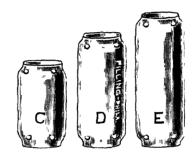


Fig 28—Glass tubes, C, D, and E, useful in acute suppurative cholecystitis, for stage operation, when fundus of gall bladder cannot be exteriorized

cock has devised a muscle-splitting incision in which the skin is divided obliquely on the line of the seventh intercostal space from the anterior axillary line to the right rectus abdominis This parallels the fibers of the external oblique muscle, which are separated, the anterior and posterior sheaths of the right rectus being divided and the rectus muscle retracted to the left. The intercostal nerves are spared In elderly or relaxed individuals the internal oblique is often found to be retracted laterally, otherwise it is partly divided, the fibers of the transversalis split, and the peritoneum opened Although Babcack has used the incision for cholecystectomy, it gives a rather limited exposure unless the abdominal wall is relaxed or the rectus divided It is ample, however, for exteriorizing the gall bladder The deeper layers of the wound are preferably united by in-

terrupted 30-gauge soft stainless steel wire tied with a surgeon's or square knot

Retraction of the gall bladder and spontaneous closure of the opening usually follow rapidly after the obstructing calculi have been removed, and the patients have left the hospital as early as the fifteenth day. About one-third or one-fourth have required a secondary cholecystectomy A persistent fistula suggests the presence of an unremoved foreign body, usually a gallstone

Routine opening and exploration of the common and hepatic ducts during operations upon the gall bladder have been emphasized during recent years It should be remembered that opening the common duct doubles the mortality from cholecystectomy even if done by competent surgeons. The surgeon of average skill will doubtless have an even higher mortality rate and should realize that there is no justification for opening the common duct unless it is large, distended, thickened or unless stones are palpated in the common or hepatic ducts by the aid of a finger passed through the foramen of Winslow Liploration through the diluted cystic duct is much less dangerous, as the end of the duct may be ligated after the procedure

It should be emphasized that the free abdominal leakage of bile after operation upon the duets is often fatal. Consequently all openings should be meticulously closed by fine sutures where they are not occluded by drainage tubes. If a rubber T tube is used it should not be so stiff as to produce pressure necrosis. There have been fatal secondary hemorphages from this cause. The removal of a wedge of rubber from the apex of the T as suggested by Orr may greatly facilitate the introduction of the tube.

In order to remove small stones Babcock has had tubular flexible probes made in graduated sizes. If they are attached to a 2 cc syringe so that salt solution may be alternately injected and aspirated, it is possible to aspirate small calcareous particles and bile mud otherwise not easily removed, and by hydrostatic pressure to distend the duct for the deeper entrance of the probe or to prove that the common duct and ampulla are permeable for liquids. The bulbous tip may be carried into the hepatic ducts Unfortunately, thin-walled ducts tend to collapse over the end of the probe on aspiration

Graduated dilatation of the common duct and ampulla by special probes has acquired some popularity, although secondary recontracture is to be expected in many of the patients. Dilating probes should be used with great care, otherwise the duct may be ruptured or perforated or a false passage made in the wall of the duodenum

Ligation of the Cystic Artery-This artery, although small, branches from the hepatic artery so close to the aorta that it has sufficient internal pressure to exsanguinate the patient if not well secured Catgut ligatures, especially if larger than 0 to 00, may slip from the end of the vessel, and unless a necrospy is performed the death may be ascribed to postoperative shock. Death may occur with the escape of little or no blood from a dramage tube or a cigarette drain Fine silk is much more reliable as a ligature for such a small vessel Cashman, however, mentions that a silk ligature used to tie the cystic duct was later found to be the nucleus of a calculus in the common duct

Drainage after Cholecystectomy—After years of closure of these wounds without drainage, a death from internal leakage of bile following cholecystectomy has emphasized the desirability of a small rubber tube drain in every case. This is removed ordinarily in 24 hours by an

attached fine wire without disturbing the other dressings and affords an added measure of security Unfortunately, it does not invariably carry escaping blood or bile from the abdominal cavity into the dressing

Biliary Fistula—In cholecystectomy, failure to expose, raise and closely hug the overhanging neck of the gall bladder has led to hundreds of divisions of the common duct with secondary leakage of bile, peritonitis, or, if the patient is fortunate enough to recover, a chronic biliary fistula or obstructive jaundice Although there is a question as to whether absolutely sterile bile in the peritoneal cavity will cause a fatal peritonitis, there is no question but that death commonly results from the free internal leakage of bile In case of doubt, even though the dressings are not stained, the wound should promptly be reopened and the leaking opening occluded or adequately drained The not infrequent secondary biliary fistula debilitates the patient and may lead to a very serious secondary operation If such a residual fistula persists for some days after the removal of all drains and it seems probable that the common duct has not been completely divided but is perhaps only obstructed, Babcock introduces the largest sized rubber tube that will enter the fistula and applies suction drainage, using a column of water about one meter in height. In such a case, usually in three or four days, the flow of bile from the tube stops entirely when the tube is withdrawn and the opening soon closes

Jaundice adds greatly to the danger of any abdominal operation. About 30 per cent of jaundiced patients will have operative or postoperative hemorrhage, and ten per cent of these patients will die despite any known treatment. Repeated blood transfusions both before and after operation on a jaundiced pa-

tient seem to be the best known treatment Injections of Ringer's or Hartmann's solution with glucose are of value, although often they do not prevent postoperative bleeding For continued free hemorrhage as many as three or four transfusions may be necessary daily Preliminary intravenous injections of calcium have not proved effective in preventing hemorrhages as was hoped. Unless the jaundice is of very recent onset or there is the lack of hemorrhagic tendency found in certain patients with cirrhotic liver, a preliminary decompressive operation should be done first A small drainage tube is tied in the gall bladder The internal end is placed 30 cm above the level of the abdomen and then lowered 2 cm every second hour so that the biliary system is gradually decompressed From ten days to three weeks later the necessary operation may be performed

Postoperative Colic and Indigestion—There are certain patients who continue to have attacks of colic after removal of the gall bladder Even a second exploration of the ducts does not always bring relief These patients may drift on to the habitual use of narcotics. It is quite possible that some of the patients have a psychoneurosis, no organic obstruction Purely empirically we have been able to obtain permanent relief in two or three cases from insulin, giving an average of ten units twice daily Most patients who have had chronic disease of the biliary tract have more or less pathologic change in the liver and should be kept on a restricted diet and given alkalies after meals, mild laxatives as required, and possibly vaccines for at least six months after the operation

Carcinoma, a common cause of jaundice with enlarged gall bladder, should always be verified by operation, as it may be simulated by gallstones or other

benign conditions. In the gall bladder, carcinoma often is associated with stones and a purulent cholecystitis without jaundice. In the early stages it is to be treated by cholecystectomy with or without the removal of adjacent portions of the liver.

Carcinoma of the common ducts, ampulla, or head of the pancreas may at times be diagnosed sufficiently early to enable radical excision. Whipple has emphasized the importance of eliminating the pancreatic juice from the field of operation This is activated by bile and the intestinal fluids with disastrous erosion. An associated choledochogastrostomy and gastro-enterostomy with ligation of the head of the pancreas should be done at the first stage in preparation for the later removal of the duodenum, the common duct, and perhaps a part of the head of the pancreas Too often the patient, through delay, drifts into an advanced moperable condition before operation is permitted

Acute Cholecy stitis

- G J Heuer⁵² believes that the literature regarding the surgical aspects of acute cholecystitis gives the impression that the clarification of certain matters often referred to might aid in determining the comparative value of early and late surgical treatment. He raises the following questions
- 1 Has not the relationship between the clinical symptoms of acute cholecystitis and the pathological course of the inflammatory process in the gall bladder an important bearing upon the question of early or late operation?
- 2 Does the acutely inflamed gall bladder so rarely undergo gangrene and perforation that these complications may be disregarded as important factors in the treatment of the disease?
- 3 Do the complications of gangrene and perforation of the gall bladder con-

tribute so little to the mortality in disease of the gall bladder and bile ducts that they may be disregarded in a plan of treatment of the disease?

4. Is the danger to the patient of operating in the acute stage of the disease before gangrene and perforation have occurred greater than the danger of gangrene and perforation, the result of a conservative or waiting policy?

In an effort to find an answer to these questions the author includes studies made of 1565 cases and, in addition, over 35,000 cases of disease of the gall bladder and bile ducts gathered from more recent literature, as well as some 1500 cases of acute cholecystitis specifically. In this article, he states the conclusions at which he arrived with respect to the questions which he propounded

He states that the clinical symptoms, physical signs, and laboratory data in acute cholecystitis often fail to indicate accurately the course of the pathological process in the gall bladder. In the acutely progressive type of the disease, the clinical manifestations fairly closely parallel the pathological process in the gall bladder, but in other cases, even in the presence of subsiding or minimal symptoms, the pathological process in the gall bladder may proceed to gangrene and perforation of the organ It appears that gangrene and perforation occur approximately in 20 per cent of all cases of acute cholecystitis, the pathological course of which is not interrupted by surgical measures It appears further that these complications are responsible, under a deferred plan of treatment, for a mortality in acute cholecystitis which varies greatly among different observers, but which in the literature is rarely below 20 per cent and often as high as 40 per cent This mortality represents approximately ten per cent of the total mortality in the surgical treatment of non-cancerous disease of the gall bladder and bile ducts.

The incidence of gangrene and perforation and the mortality are sufficiently high not to be disregarded in a plan of treatment of this disease, unless it be true that they are less a menace to the life of the individual with acute cholecystitis than operation performed early for the purpose of avoiding them That these conditions are not less dangerous but distinctly more dangerous than operation in the acute stage of the disease is suggested by an experience derived from a study of 153 cases of acute cholecystitis in which operation in the acute stage was deliberately planned and, so far as possible, consistently carried out with the purpose of attempting to lower the mortality from gangrene and perforation of the gall bladder In this series. the total mortality was 32 per cent, but when analyzed from the viewpoint of the extent of the disease, the mortality in 137 cases in which cholecystectomy was performed before perforation occurred was 21 per cent. The mortality in 16 cases subjected to operation after perforation had occurred was 125 per cent This mortality is so favorable in comparison with the published statistics of mortality rates following the surgical treatment of cholecystitis that the author feels justified in continuing a method of treatment which is opposed to the conservative method

C G Heyd⁵³ in an editorial ("Acute Cholecystitis"—Why Delay) maintains that the early history of appendicitis was clouded by similar controversial discussions as to when and when not to operate For the physician to counsel waiting in acute disease is to participate in a surgical gamble that "under a regimen of starvation, local applications, an ascending phase of pathological change will

become arrested" This is distinctly a gamble with the odds against him. The records of patients so treated show that while nature may "wall off" the gall bladder the primary and essential lesion is, in over 63 per cent of cases, a continuing process leading to grave surgical complications

Few individuals will long withstand the disseminating effects of the retention of the products of infection under pressure and the technical indication for operation in acute cholecystitis is to institute drainage, so that the products of infection will not be retained under pressure, hence gangrene and perforation will be forestalled. Operation provides a means of overcoming the increasing peril of undrained infection. It is not necessary to advocate cholecystectomy or any one set form of operation The indication is to operate carefully, with due celerity, relieve the mechanical obstruction, and provide drainage This may be done by a simple cholecystectomy, by marsupialization of the fundus of the gall bladder, or by splitting the gall bladder from the fundus to the cystic duct and enucleating the mucous membrane of the gall bladder, performing an intravesical cholecystectomy with drainage By any one of these procedures drainage is provided, yet the protective barrier around the gall bladder and particularly that protection interposed between the liver and the gall bladder is left undisturbed

Few will countenance the classical cholecystectomy with the opening up of the large liver bed of the gall bladder fossa, thus exposing a relatively wide area to septic absorption and destroving the natural barrier of resistance that has been built up. Most of the cases of acute cholecystitis are superimposed upon chronic cholecystitis and usually with the complicating factor of calculus. Preventive medical thought and wise, ju-

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dicious surgery would suggest the early removal of the chronically infected gall bladder and not delay until the accident of infect on initiates a fulninating acute cholecystitis. If infection is the primary and basic danger in acute gall bladder disease then the continuation of the infection by a policy of "innocuous desuetude" is harmful and lethal and any properly collected series of cases will show a higher mortality with this policy than that which accompanies early surgical intervention

Teachers of surgery who lend their prestige and give support to a policy of waiting provide authority for timid surgeons, inexperienced operators, and procrastmating practitioners. Increasing statistics demonstrate forcibly that the operative mortality in patients who are operated upon in the early stage of acute cholecystitis is not greater than that which obtains in routine gall bladder surgery. Furthermore, the high mortality, of approximately 20 per cent that occurs after late operation is largely the mortality that arises from the complicationsempyema, abscess gangrene, and perforation-and, when and if operative recovery finally takes place there remains the permanent damage to liver and associated organs with continued morbidity

Mortality—In discussing mortality in acute conditions of the gall bladder, F. Taylor⁵⁴ grouped 129 cases according to morphologic observations in the gall bladder as acute edematous, acute suppurative and acute gangrenous. In analyzing the signs and symptoms of patients from these separate groups, it was found that there was no definite criterion by which they could be differentiated. There was a marked overlapping of signs and symptoms of patients with the acute edematous type, from which no complications might be expected, with the other

two more serious groups. But one aid in making this differentiation was noted the white blood cell count This, in general, varied directly with the severity of the lesion However, it was misleading and bore no relation to the pathologic condition in more than ten per cent of The clinical features of the the cases disease often bear no relation to the severity of the pathologic process. The mortality for the entire series was 163 per cent Patients operated on the first four days after acute onset gave a mortality of approximately five per cent ()f those operated on five or more days after onset, 23 8 per cent died. The perforating and gangrenous lesions have a higher incidence in those of advanced years Therefore, age is no excuse for delaying operation More than half the cases may be expected not to improve or become worse while being observed in the hospital. No case is so urgent that preoperative administration of adequate amounts of dextrose solution can It would seem best to be neglected remove an occasional edematous gall bladder, in the doubtful case rather than run the risk of the more radical policy of watchful waiting

Cholecystectomy

Technic—An operation based on the clinical experience of H P Ritchie⁵⁵ to meet the requirements of complicated situations in gall bladder surgery is described with arguments in support of the procedure, as follows

- 1 Speed of achievement
- 2 The assurance to the surgeon of an ineffable satisfaction in the knowledge that no damage has been done to structures outside the field. The plan of excision erases the possibility of injury to the liver and the danger of secondary hemorrhage.

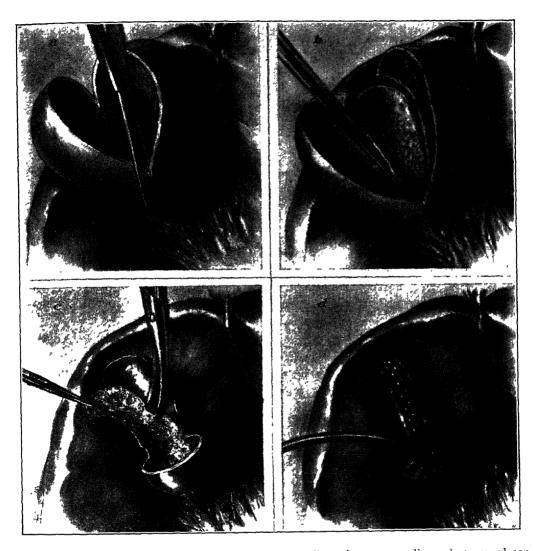


Fig 29—a and b These incisions should be carefully and symmetrically made to avoid confusion of direction and extent c, I asked Miss Hirsch of the Art Shop to make the picture of the ladle diagrammatic. The surgeon will visualize all sorts of combinations of width of handle and depth and irregularities of the cup. I think enough of the handle should be left to insure its suture into a cord and enough of the cup be left to allow suture about the drainage tube. I suggest the surgeon try out the dissection of the mucous membrane on those cases where the gall bladder had been removed by formal methods. d, It has been suggested that the tube be brought up through the handle. So far this has not been done. (Courtest Surgery, April 1937.)

- 3. It meets the first principle of any plan for cholecystectomy, the removal of the mucous membrane
- 4. It provides drainage of the biliary system for cases of suspected pancreatitis
- 5 It leaves a valuable guide to essential structures should a second attack on this field be indicated

Complications of Gall Bladder Surgery—These may be classified as (1) mechanical, (2) chemical, (3) metabolic, and (4) infectious C G Hevd⁵⁶ points out that the complications that occur within the first 24 hours after operation are obviously those that are associated with hemorrhage, gastric dilatation, embolism, pulmonary collapse and cardiac The early complications are dilatation those that arise from mechanical or infectious causes, such as intestinal obstruction, volvulus, pyloric occlusion, peritonitis (local or general), subphrenic abscess or retroperitoneal phlegmon From the purely chemical standpoint certam complications occur Some are secondary to continuous and repeated vomiting, such as alkalosis, hypochlotenna, and hypohydration also the acidosis from intractable diarthea, and the complications of obscure or perverted liver activity -- "liver deaths"

Complications occurring after cholecysectomy or cholecystostomy are different from those that arise from surgery of the common duct. The author analyzed 557 personal cases, both ward and private, in which laparotomy was performed for diseases of the gall bladder or the external biliary-duct system He asked himself the following questions many of these patients survived surgery? And in those who died, what was the mechanism of death? Were the preoperative preparation, the surgical intervention, and the postoperative therapy competent and adequate? Furthermore, could any reasonable deductions be made that would help prevent the complications and mortality in any future group of patients? All the patients were operated upon by the author himself. A better showing could undoubtedly have been made if the analysis had been confined to private patients alone. It seemed wiser to take the total number because the conclusions could then be applied to the gall bladder service of any general hospital

Of the 557 patients, 417 were private and 140 were clinic cases. Of the 417 private patients, 20 died (a mortality of 48 per cent). Of the 140 clinic patients, 19 died (a mortality of 135 per cent). This noteworthy difference in the mortality rate between the two groups is due to the greater degree of pathological damage in the clinic patients from delay in seeking surgical intervention.

Cholecystectomy is one of the safest of all intra-abdominal operations for chronic gall bladder disease, and in the hands of a reasonably well trained surgeon is relatively free from postoperative complica-Operations upon the bile ducts or gall bladder in the presence of acute inflammation are associated with greater technical difficulties and a very marked increase in the frequency of complica-In 500 uncomplicated cases the mortality was 3.3 per cent but in 34 cases in which cholecystostomy was done for acute cholecystitis, there were five deaths, or a mortality of 147 per cent Pancreatitis was observed in 21 cases in the series, and death resulted in five, a mortality of 238 per cent There were 13 malignancies of the gall bladder or All of the 13 patients were jaundiced and all had gallstones Gallstones were present in 592 per cent of all the cases in the series. The average age of the patient at operation was 404 years, the youngest was eight and the oldest, 79 Fifty-nine of the patients had ulcer of the stomach or duodenum associated with the gall bladder disease

Of the 39 deaths in the series of 557 cases there were eight which could not be attributed to the usual causes. In two of the cases hyperpyrexia and coma followed surgical intervention very shortly and progressed until death. In three cases of obstructive jaundice coma developed and the patients died. In three others pronounced cardiorenal collapse developed and the patients died in from 24 to 36 hours.

The author believes, after due consideration of the factors involved (the type of lesion, the biological background of the patient, the adequacy of surgical intervention, the complications and the mortality), that surgical treatment of gall bladder disease is safe and highly satisfactory

Perforation of Gall Bladder—A series of 46 perforations of the gall bladder which occurred in 886 operations for cholecystitis, a percentage of 52, is being reported by R L Sanders⁵⁷ as a further argument for recognition of the high incidence of the complication and the urgent necessity for operation before its development

The proper time for operation in acute gall bladder disease has been much disputed The main difficulty in Sanders' opinion, is determining whether the condition is or is not acute. Even the keenest diagnostic acumen is fallible in discerning perforation in many instances Those authors who have mentioned the matter have admitted that their preoperative diagnosis was correct in comparatively few cases of perforation of the gall bladder As has been stated often, the symptoms are so variable in number and intensity that no certain syndrome can be regarded as pathognomonic of rupture until its devasting consequences become

almost irreparable. Several cases of this series are proof that an acute perforation may be found when no history of an acute exacerbation of symptoms is given and the patient's condition is not extreme at examination. A scout film of the abdomen or fluroscopic study may afford a clue to the diagnosis in revealing the presence of stones in the region of the gall bladder, but this is not entirely dependable. We know that perforation can and does take place when no stones are present. The four cases of gangrene with perforation mentioned in this series are examples.

Cases of chronic perforation are recognizable, as a rule, by a history of unchanging, more or less severe symptoms over an extended period There is no need for delaying operation here When acute symptoms have begun to subside, surgery should be postponed until further regression takes place But if the patient's suffering is unduly prolonged or is increased, the condition may be considered acute, requiring immediate opera-Prompt surgery is indicated, of course, when persistent nausea and vomiting, weak pulse, increased respiration, an elevated leukocyte count, marked tenderness, and excruciating pain point to rupture into the peritoneal cavity

In deciding the most opportune time for surgery, therefore, we can be guided only by present signs and symptoms. Operation may be elective in the apparently chronic cases, but it is imperative and urgent if symptoms already pronounced remain unchanged or become aggravated. Surgery may be postponed for a few days when there is evidence that the symptoms are subsiding or a possibility that they may do so under treatment. Sanders agrees with Behrend that, under proper control of a capable surgeon, there is little danger that an acute case of cholecy stitis may go on to

perforation; an exacerbation of symptoms may be readily detected and operation performed without delay

It is generally conceded that cholecystectomy is the procedure of choice in gall bladder disease, when feasible. One material advantage of allowing acute symptoms time to subside lies in the fact that cholecystectomy usually may be done in the subacute stage, obviating probable necessity for second operation

In acute cholecystitis, when removal of the organ is contraindicated. Heyd and others have employed the method of bisecting the gall bladder from fundus to duct, enucleating the mucous membrane, inserting a tube, and closing the gall bladder about it. Heyd states that cholecystectomy is too dangerous and cholecystostomy alone often leads to the necessity for a second operation because of retention of an infected mucous membrane Behrend believes the formation of adhesions the principal source of danger in a second operation. Both of these factors contribute to the hazard of cholecystectomy after cholecystostomy

As was stated in the beginning, the whole purpose of this discussion is to dispel the illusion that perforation of the gall bladder is a negligible possibility and to bring to mind more forcibly the poor prognosis after its development. It is difficult to comprehend why, considering the dangerous potentialities patients suffer with gall bladder symptoms for years before obtaining permanent relief. The fault cannot be attributed wholly to ignorance on the part of patients. Surely, many more are exammed than are relieved. The responsibility lies with us, then, who realizing after a reasonable length of time that medical treatment is not curative, fail to see that our patients receive the benefit of surgery before the disease process progresses too far An awakened conscientiousness on the part of medical men would seem to be largely effective in reducing the necessarily high number of perforated gall bladders and the appalling number of fatalities in their train

Tumors of the Gall Bladder

Benign tumors rarely occur in the gall bladder E Simon⁵⁸ states they may be myomas, fibromas, and adenomas Occasionally cystadenomas which develop from the ducts of Luschka are seen Cysts may also be produced by the echinococcus, as shown in one case Tumors of the gall bladder are almost always malignant, usually carcinoma Carcinoma limited to the gall bladder is seldom observed, and when it is, metastases usually appear shortly after surgical treatment Roentgenological visulization of the gall bladder does not permit the early recognition of carcinoma, usually the gall bladder carcinoma has already extended to adjacent structures Often, however, the apparent carcinomas are inflammatory processes. Gall bladder carcinoma may develop after cholecystos-An interesting case is described in which one and one-half years after the removal of pus and stones with subsequent dramage an moperable carcinoma was found. The association of gallstones and carcinoma of the gall bladder was demonstrated in from 70 to 80 per cent It is believed that gall of the cases bladder carcinoma arises as any other carcinoma, but that its development is favored by the presence of stones Carcinoma is particularly likely to develop in a chronically inflamed, stone-containing gall bladder. About five per cent of all patients with gallstones develop carcinoma later This leads to the conclusion that early operation should be performed for gallstones, particularly when the stones occur in patients of cancer age

COMMON BILE DUCT

Congenital atresia of the bile ducts is a rare condition, but E J Donovan⁵⁹ states that they have had 16 cases at the Babies Hospital during the past ten years Although this is a small group when compared with 21,000 admissions during the same period, these cases have occurred frequently enough to justify reporting them He has two other cases which were operated upon at St Luke's Hospital to add to this group

The exact etiology of this condition is unknown, and while many theories have been advanced to explain its cause, the most plausible one apparently is that the obliteration of the bile ducts is due to a failure of the ducts to canalize during development, and the accompanying cirrhosis of the liver is secondary, resulting from the obstruction to the outflow of bile. This theory easily explains the findings in many cases.

In making the diagnosis of congenital atresia of the bile ducts, it is necessary (1) Icterus neonatorum, to eliminate which usually disappears before the patient is two weeks old, (2) syphilitic hepatitis, which may be excluded by serology of the patient and his parents in the absence of other stigmata of syphilis, (3) congenital hemolytic icterus, which is rarely found in such young children, may be excluded by a normal tragility of the red cells, (4) jaundice of sepsis, which may be ruled out by the absence of fever, and by negative blood culture and the absence of other signs of sepsis, (5) jaundice due to pressure on the common or hepatic ducts by enlarged lymph nodes Donovan has had one case who had a typical history of atresia of the bile ducts who was successfully operated upon for obstruction of the common duct Autopsy four months later showed the common duct

obstruction to be due to tuberculosis of the hepatic lymph nodes

The aim of surgery in these cases is to deliver the bile into the intestinal tract, and any operation which may accomplish this is worth while. Cholecystgastrostomy and cholecystoduodenostomy are excellent procedures if there is enough of the duct system present to effect such an anastomosis If not, drainage to the outside may be established, creating an external biliary fistula which may later be implanted into the stomach or duodenum Saline should be injected into the ducts at operation in hope that the obstruction may be due to a mucous plug which may be forced out Obviously all of these cases deserve an exploratory celiotomy, hoping that there is enough of the duct system present to do some of the above procedures

Abnormal Function of Common Bile Duct

According to W. Walters, 60 this is largely a matter of infection and obstruction associated with biliary calculi and other benign obstructive lesions of the biliary tract, such as pancreatitis and cholangeitis, stricture of the common bile duct and abnormal function of the sphincter of Oddi

The high incidence of stone of the common duct associated with cholelithiasis leads one to assume that, in many cases, stones of the common duct are being overlooked. This possibility could be reduced to a minimum if all dilated common bile ducts were opened and explored for stones even though stones could not be palpated through the walls of the ducts.

Introduction of a T tube into the common bile duct for drainage following exploration has allowed study of the size and rapidity of emptying of the common bile duct (choledochography, cholangio-

graphy) Such roentgenologic studies reveal the presence of persisting obstruction and indicate their cause, such as inflammatory thickening in the head of the pancreas, abnormal function of the sphincter of Oddi and overlooked stone in the common duct. In a recent case, in which a stone persisted in the common duct, fragmentation of the stone and forcible expulsion of it into the duodenum

sphincteric mechanism at the lower end of the common bile duct, reduced the intraductal pressure and relieved pain

Abnormal function of the sphincter of Oddi usually occurs secondarily to retention of stones in the common bile duct and pancreatitis but in a few cases it may occur independently. Acute and subacute inflammatory changes in the gall bladder progress through the walls of

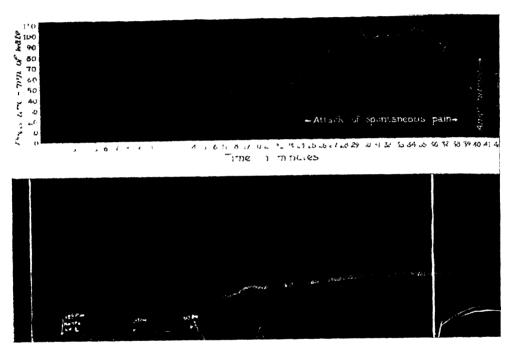


Chart 1—(Above) Showing increase in intraductal pressure during an attack of pain (Below) Precipitation of biliary colic with increase in intraductal pressure by the administration of morphine (Courtesy Annals of Surgery, October 1937)

occurred after introduction of ether and alcohol into the common duct after the sphincter of Oddi had been caused to relax by administration of anyl nitrite

Studies indicated that pressure of as much as 160 mm of water occurred within the common bile duct during an attack of biliary colic. In some cases such an attack can be precipitated by administration of morphine, ½ grain (001 Gm.). During the attacks of pain the use of an antispasmodic substance, nitroglycerin or amyl nitrite, has relaxed the

the common bile duct and through the lymphatic channels into the pancreas and liver, producing jaundice without stones of the common duct in approximately ten per cent of cases. Removal of the infected gall bladder and drainage of the common bile duct not only have removed the source of infection in the gall bladder but infections in the pancreas and liver have subsided secondarily.

Choledochography, in these cases, has been of the greatest assistance in determining the propitious time to remove

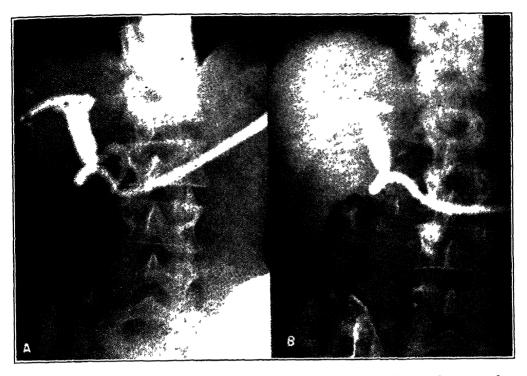


Fig 30—A, Choledochogram showing dilatation of the common bile duct, with stasis and narrowing of the lower portion from persisting pancreatitis B, Choledochogram shows retention at end of ten minutes (Courtesy, Annals of Surgery, October, 1937)

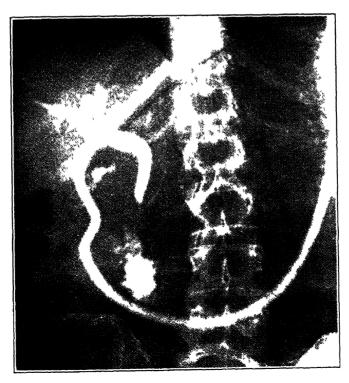
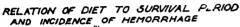


Fig 31—Choledochogram showing dilatation of ducts with reflux of opaque media up pancreatic duct. Patient had been operated upon for biliary colic. Pancreatitis was found, there was no stone in the common duct. (Courtesy. Annals of Surgery, October, 1937.)

the T tube from the common bile duct On several occasions in which it was thought that drainage had been of sufficient duration, choledochograms gave evidence of persisting enlargement of the common bile duct, with delay in its emptying Reflux of the opaque sub-



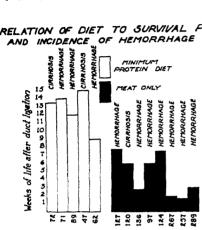


Chart 2-Illustrates the effect of a diet high in protein upon the period of survival and the incidence of hemorrhage in jaundiced animals. Each column represents one jaundiced dog. The white columns represent dogs given a low protein diet and the black columns those which were given meat only The cause of death is indicated above each column (Courtesy Annals of Surgery, October 1937 i

stance into the pancreatic duct has been demonstrated

Jaundice

The cause and prevention of the bleeding discrasia is discussed by H C Nattziger et als 61. Their experiments have established the fact that, in the presence of jaundice, there is an alteration in the sultur metabolism of animals and human beings. An important feature of this alteration is the retention in the circulating blood of sulfur compounds which are anticoagulants That only minute quantities need be retained to alter coagulation is shown by the fact that small doses of the purified product, such as cystems or methionine, produce a marked effect in vivo, and minute amounts will alter coagulation in vitro

An important secondary feature affecting the concentration of these products is the condition of the kidneys Sulfur compounds normally excreted by the liver as cystine, taurine and taurocholic acid are shunted through the kidneys The sudden rapid rise in blood sulfur with the onset of jaundice in animals given mercury showed experimentally that the threshold for excretion of these products is raised by damage to the kidneys

Clinically it is well known that a jaundiced patient's chances of survival are jeopardized by poorly functioning kidneys, and that jaundiced patients given mercury compounds such as salvrgen are particularly likely to bleed

That the source of the anticoagulant material is metabolized protein, both exogenous and endogenous, is shown by the fact that jaundiced dogs fed meat alone, on which normal dogs thrive, lived

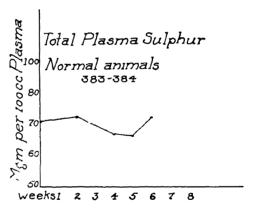


Chart 3-The total plasma sulfur of two normal animals remained at approximately 70 mg per 100 cc for a period of six weeks (Courtesv Annals of Surgery, October, 1937)

only one-third as long as those allowed a minimum of protein, and nearly all succumbed to massive hemorrhage It seems important that, in patients with obstructive jaundice, the intake of protein should be kept at a minimum during the period of preparation for surgery Furthermore the metabolism of body protems should be minimized by rest in bed and the administration of sedatives

Feeding of excess carbohydrate and the administration of glucose intravenously decrease the metabolism of protein. The output of bile salts from a biliary fistula is reduced to a low level when the animal is starved, but it is still further reduced when carbohydrate only is fed. That the giving of glucose has other important beneficial effects than than these is not doubted.

An excess of calcium chloride appreciably inactivates sulfydryl anticoagulants in vitro. Its use in patients with jaundice is based on the belief that it has the same effect in vivo if it is administered in sufficient quantity.

The benefit to be derived from infusion of normal blood is obvious, but the difficulty of replacing a sufficient quantity of blood presents itself

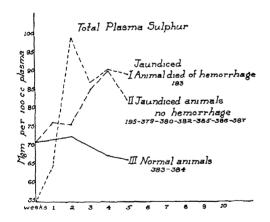


Chart 4—Shows the rapid rise of the total plasma sulfur in jaundiced animals. An animal which died of hemorrhage shows the most marked rise (Courtesy, Annals of Surgery, October, 1937)

The advantages of gradual decompression following complete common duct obstruction are outlined by I S Raydin and W D Frazier 62 For some years the authors have been interested in the pathologic physiology of common bile duct obstruction They describe changes

in the liver cells and the effect of portal stasis on the circulation resulting from biliary obstruction. They also describe dangers of rapid release of obstruction of the common bile duct and describe a method which provides for gradual decompression.

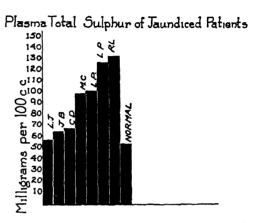


Chart 5—Each column represents the total sulfur level of the whole plasma of a jaundiced patient as compared with the average normal One patient (L P) with a total of 125 mg per 100 cc died of hemorrhage following removal of a stone in the common duct (Courtesy, Annals of Surgery, October, 1937)

As soon as the T-tube has been sutured in the common duct and bile begins to flow from it, it is clamped. When the patient returns to the ward, the clamp is removed and the tube is connected to the sterile decompression apparatus (Fig 32) If a cholecy stostomy has also been performed, the gall bladder tube is attached to a similar apparatus. The apparatus board is so fastened as to put the lowest hook approximately on a level with the common duct. The distance between the hooks is approximately 5 cmm For the first 12 to 18 hours after operation the Y-tube is hung on the top hook approximately 25 cmm above the level of the common duct The usual result is that only a little bile is forced over into the drainage bottle with respiratory movements The Y-tube is then moved down-

ward but if, at this level, a large amount of bile is drained externally, this can be lessened by raising the tube again. By thus adjusting the level of the apparatus, the amount of bile drained externally can be regulated. Enough is obtained daily for analytical studies and the remainder is forced down into the duodenum by controlling the level of the Y-tube. To do this the level must be changed from time to time to compensate for changes in the condition of the common duct and the tonus of the sphincter of Oddi

biliary ductal system must be clear from the cytologic and physiologic point of view, there are additional advantages of no mean importance. The forcing of bile into the duodenum, once the obstruction is relieved, which prevents the loss of bile to the exterior, is of great value

It is only necessary that the pressure from the decompression apparatus be sufficient to overcome the tonus of the sphincter mechanism at the lower end of the common bile duct for the bile to flow freely into the duodenum

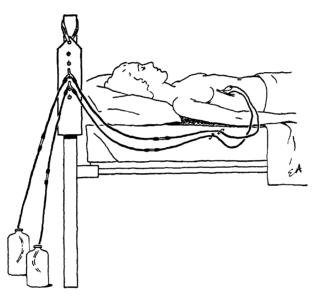


Fig 32—Diagram of decompression apparatus (Drs I S Ravdin and W D Frazier The Advantages of Gradual Decompression Following Complete Common Duct Obstruction Surgery, Gynecology and Obstetrics, July, 1937)

Thus, as the postoperative traumatic edema of the ductal wall subsides, the level can be lowered, but in order to overcome the sphincter tone, a certain amount of pressure must always be maintained by keeping the Y-tube on the second or third hook. That the bile is passing into the duodenum can readily be determined by frequent observations of the patient's stools and repeated van denBergh determinations.

While the advantages of gradual decompression of a chronically distended Formerly, the method of simply allowing the bile to drain into a bottle hung at the side of the bed exerted, if anything, a suction effect. In many cases this resulted in the drainage of large amounts of bile

The loss of fluid and electrolytes when the bile is thus drained to the exterior is considerable, but of even more importance is the loss of the intestinal functions of the bile

While the externally drained bile may be returned to the patient through a Jutte

tube into the stomach, it is often impossible to administer all the bile drained externally by this method and the procedure is distasteful to the patient. In the method which the authors advocate, the bile enters the duodenum by its normal route. Appetite improves rapidly and "pancreatic asthenia" has not been observed during convalescence.

Biliary Fistulas

Treatment - According to W W. Babcock, 63 persistent fistulous openings following drainage of the gall bladder usually discharge clear mucus, if a mucocele or hydrops of the gall bladder is present, or mucopurulent material, if due to a gallstone impacted in the neck of the gall bladder or cystic duct, or to a carcinoma If the mucocele is a result of stenosis of the outlet, the gall bladder should be removed or the lining mucosa completely destroyed A stone impacted in the neck of the gall bladder often may be removed without hospitalization of the patient The fistulous tract is first enlarged by daily insertion of rubber tubes of increasing caliber, or by firm gauze packing, until a channel of sufficient size is formed to the point of The calculus may then be obstruction detected with a probe or seen through a Kelly cystoscope or a urethroscope, dislodged by scope or forceps, and removed. At times it is necessary to incise cautiously, or partially to destroy dense scar tissue overlying the stone The latter may be accomplished by the application of small cotton swabs lightly moistened with a ten per cent solution of chloride of zinc If this powerful erosive is used, little should be applied and attempts to remove the stone delayed for 24 to 48 hours, during which time a firm, dry gauze packing is left in place. To reduce the size of the exposed impacted stone, cotton swabs wet with ether may repeatedly be

applied until sufficient cholesterin has been dissolved from the stone to enable its fragmentation, dislodgement, and extraction. With all obstruction removed the fistulous tract usually closes permanently within a few days. It is to be remembered that an acute or subacute purulent cholecystitis with gallstones is not uncommon in an unsuspected cancer-

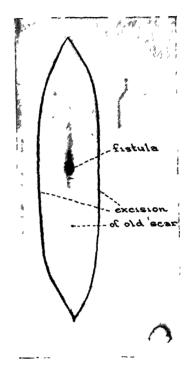


Fig 33—Line of excision of old scar after delineating fistulous tract by the injection of ethereal solution of methylene blue (Dr W Wayne Babcock A Simple and Effective Method for the Closure of Biliary Fistulas, in Surgery, Gynecology and Obstetrics, July, 1937)

ous gall bladder Twice after the calculi had been removed and the mucopurulent fistula closed, has Babcock seen a cancer later develop in the abdominal scar

Persistent partial leakage of the bile after cholecystectomy or the withdrawal of a drain from the cystic ducts usually indicates some type of obstruction in the ducts. In such a case Babcock fits a rubber tube snugly in the fistulous channel and connects it with a Wangensteen

or Pratt aspirator Usually within 24 or 48 hours the flow of bile ceases when the tube is removed and the opening is permitted to close

Fistulas following cholecystectomy or operation upon the biliary ducts from which all bile is discharged are much more troublesome and serious. From

not been removed Occasionally the fistula follows a cholecystostomy and is due to obstruction of the common duct

Irrespective of cause and at times despite the retention of average weight, the patient may be a poor subject for any prolonged intra-abdominal operation. To attempt to anastomose a divided duct

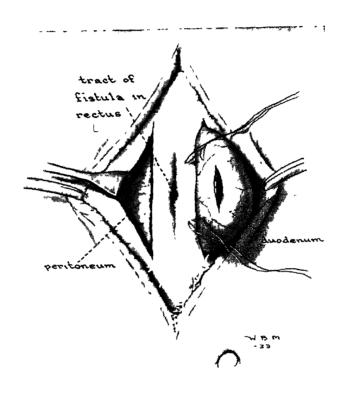


Fig. 34—The scar and subcutaneous tascia have been removed, thus exposing the sheath of the right rectus muscle with the fistulous opening. Parallel incisions have been made through the muscle on either side of the fistulous tract. Through the medial incision the duodenum has been withdrawn and sutured to the anterior sheath of the rectus. After completion of this suture line the margins of incision in the duodenum are to be sutured about the fistulous opening. (Dr. W. with Babcock. A Simple and Effective Method for the Closure of Biliary Fistulas, in Surgery, Gynerology, and Obstetrics, July, 1937.)

the constant loss of liquid, electrolytes and the impaired intestinal absorption, the patient tends to develop an increasing cachesia with impaired ability to withstand a serious operation. Usually the fistula has resulted from an accidental division to the common duct during a cholecystectomy or the common duct may have been drained but a more distal obstruction to the flow of bile has

or to unite the proximal end of an obstructed duct with the duodenum or stomach is a hazardous procedure. It is simpler to mobilize the abdominal fistula and to turn it into the adjacent duodenum or stomach, but the liberation of the fistulous tract is not always easy and the tract, when separated from its source of blood supply, may necrose and the anastomosis may fail

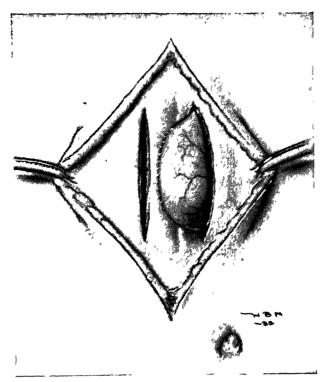


Fig 35—The withdrawn duodenum is further sutured over the anterior sheath of the rectus by completing the outer row of encircling suture (Dr W Wayne Babcock A Simple and Effective Method for the Closure of Biliary Fistulas, in Surgery, Gynecology and Obstetrics, July, 1937)

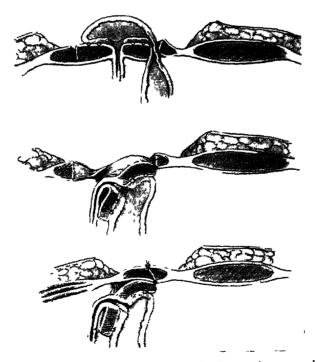


Fig 36—The top sketch illustrates the withdrawn duodenum (or stomach) united to the split rectus muscle over the fistulous channel. In the middle sketch, the segment of rectus muscle is so rotated that the attached portion of duodenum (or stomach) has been returned to the peritoneal cavity. In the bottom sketch, the margins of the anterior and posterior sheaths of the unused part of the rectus muscle have been united by suture. (Dr. W. Wayne Babcock. A simple and Effective Method for the Closure of Biliary Fistulas, in Surgery, Gynecology and Obstetrics, July, 1937.)

The following method which Babcock has used for several years has been found to be an effective and relatively superficial operation which at times may be performed even without opening the free peritoneal cavity. It is important that the operation be delayed for two or three

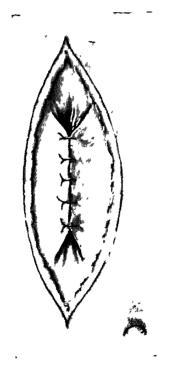


Fig. 37—Closure of the anterior rectus sheath over the rotated and depressed segment of rectus. (Dr. W. Wayne Babcock: A Simple and Effective Method for the Closure of Biliary Fistulas in Surgery, Gynecology and Obstetrics. July. 1937.)

months, or until the fistulous tract has become well organized and established During this time the escaping bile may be collected and returned to the body through a duodenal tube, drunk in grape juice, or desiccated and given in capsule If the escaping bile is purulent or contaminated, fluids, bile salts or ox gall are administered daily by mouth

The operation may be done readily under local anesthesia. After delineation of the fistulous tract by the injection of a small quantity of ethereal methylene blue solution, the old scar with its contained segment of fistula is excised to the outer sheath of the rectus Two vertical incisions five to seven centimeters long are now made through the rectus muscle, one about two centimeters medial, the other about two centimeters lateral to the The medial incision fistulous opening is deepened through the posterior sheath and peritoneum and the pyloric end of the stomach or duodenum, whichever happens to be the more accessible, is exposed, withdrawn through the wound, and opened The small opening made is applied over the fistulous channel where it is held by two encircling rows of continuous or interrupted sutures uniting the serous surface of the duodenum to the outer sheath of the rectus There is less danger of wound infection and separation if interrupted sutures of very fine (No 35 B and S gauge) annealed alloy steel wire are used for suturing and tied in a square or surgeon's knot

The vertical double pedicled flap of muscle with its contained fistula and attached stomach or duodenum is now rotated about 180 degrees to the left where it is fixed by suturing the lateral edge of its anterior sheath to the inner sheath of the adjacent medial segment of the rectus. Over the rotated flap the lateral and medial edges of the anterior sheath of the nonrotated portions of the rectus are united and the skin and fascia closed, preferably with No 32 and No 30 annealed stainless steel wire which may be buried in the anterior abdominal wall without secondary irritation Postoperative adhesions may render it unnecessary to enter the free peritoneal cavity during this operation. As the retained fistulous tube is not disturbed or separated from its blood supply, necrosis is not to be feared In several patients so operated upon, recurrence of the fistula or jaundice has not followed While chiefly employed to provide a permanent by-pass for the bile to the alimentary canal, the operation may also be used as a temporizing or stage measure.

INTESTINES

Diverticulosis of the Small Intestine

Two varieties of diverticula occur in the intestinal tract, the acquired and the congenital When all the layers of the Pathogenesis — The two important factors in the pathogenesis are a point of lower resistance where the blood vessel enters the intestine, and an increase in the intraintestinal pressure. The development of the latter is explained on the basis of irregular intestinal contractions. According to this theory, a portion of the bowel relaxes while the segments on either side are contracting. These contractions force the mucous membrane into the gap

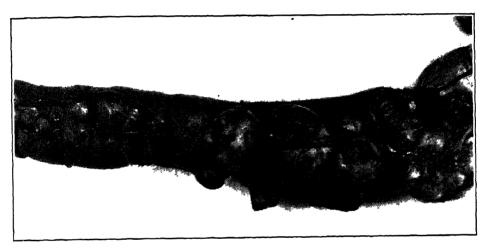


Fig 38—Portion of small intestines removed from Case 1. All sizes of diverticula are present. The relation to the blood vessels is shown in several places. The point of origin on either side of the mesenteric line is clearly shown near the midportion. The medium-sized diverticulum on the left is of the bilobed type. On the extreme right is one of the few diverticula in the whole specimen removed that extends across the mesenteric line and thus was formed by fusion of two smaller diverticula, originally on both sides of the mesenteric line. Note the increased diameter of the bowel in the region of the larger diverticula. (Courtesy, Surgery, April, 1937.)

normal intestinal wall are present in the diverticulum, it is called a true one The familiar Meckel's diverticulum is a true congenital diverticulum. The acquired variety are of the mucous membrane hernia type and have little or no muscular fibers in their walls. This type of false diverticula may occur in any portion of the gastrointestinal tract, but it is most frequently found in the sigmoid and duodenum. This paper concerns the infrequent, acquired diverticula that occur in the small intestine.

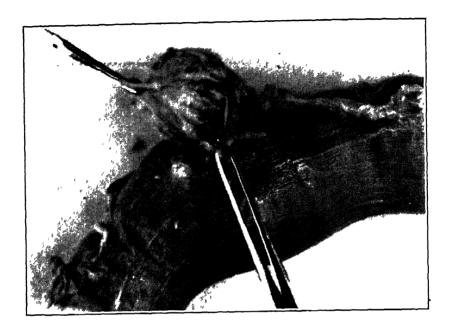
where the blood vessel enters in the relaxed segment

Acquired diverticula of the small bowel are usually multiple, occur on the mesenteric border, and arise in the upper portion of the jejunum

D Guthrie and F A Hughes, Jr. 64 report three cases The common findings were the sex, all were males, the age, 54 years of age or older, and the type of diverticula found. The first patient had the most advanced pathology and was the oldest, his age was 70

years, he had 70 diverticula in 60 inches of small bowel. A duodenal ulcer and diabetes mellitus were coexistent in the second case. The third was one of these

rectal bleeding was the chief complaint Further, the operation was the ideal procedure of resection and anastomosis, and the patient is now in perfect health. Two



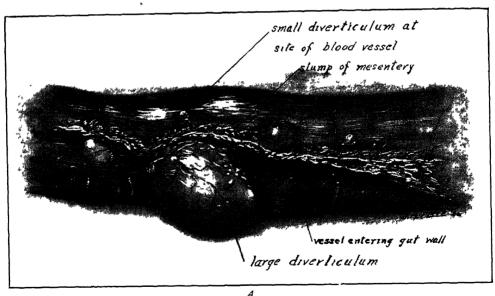


Fig 39—Portion of specimen from Case 1. The clamp and forceps are attached to the blood vessels. Several vessels are in relation with the large diverticula, only one with the small ones A, Variety of symptoms shown by above reported cases. (Courtesy, Surgery, April, 1937.)

rare cases where a diagnosis could be made by roentgen examination, and thus a diagnosis was made before operation This case was also rare in that profuse of these patients had a mucous diarrhea before admission, and all three had some derangement of the function of the upper intestinal tract after operation The authors are inclined to the belief that this latter manifestation is in favor of the theory of Edwards that irregular intestinal contractions play a part in the etiology of the formation of diverticula

Complications—The complications of diverticulosis are diverticulitis, hemorrhage, perforation, intestinal obstruction, and enterolith formation The developtearing of a blood vessel when the diverticula become excessively distended The inflammatory process may involve the serosa which then becomes sealed to the surrounding structures and causes a partial or an acute intestinal obstruction; or the process may rapidly erode through the wall, perforate, and cause a general peritonitis. The material that



Fig 40—Case 1 Portion of jejunum (five feet) removed (Courtesy, Surgery, April, 1937)

ment of these conditions may be as follows. Infected material enters the diverticulum from the bowel where it becomes shut off. The prolonged contact with the mucous membrane which has its blood supply impaired due to the ballooning, favors the development of an inflammatory process. This process may erode a vessel, resulting in hemorrhage. The hemorrhage may also result from

enters the diverticula may become hardened and form an enterolith

Diagnosis—A diagnosis from clinical examination alone has not been done A diagnosis preoperatively is possible when the diverticula fill partially or completely with barium, presenting a ball of barium as described by Case The diagnosis in Case 3 was made upon the film shown in Fig. 41. The barium

balls are evident. Most cases are discovered at operation or diagnosed at post-mortem examination

Treatment—The treatment is surgical. The process begins in the sixth decade and is gradually progressive. The only possible means of relieving

necessitate a less radical procedure. Simple excision of the diverticula or a sidetracking operation may be done.

Regional Ileitis

There are two clinical types of *regional ileitis* (1) The involvement of a rather



Fig. 41—Case 3. Roentgenogram taken five hours after barium meal, showing retention of barium in several diverticula. (Courtesy, Surgery, April, 1937.)

symptoms caused by diverticula is the removal of the diverticula *Resection* of the involved portion of bowel is the ideal procedure. The extent of the process or the location of the diverticula may

short, localized segment, which usually consists of a single lesion, and (2) a similar process which involves longer segments and usually consists of multiple lesions. J. de J. Pemberton and P. W.

Brown⁶⁵ state that pathologically, both types differ grossly in extent, but microscopically both are associated with the same granulomatous process and tend to destroy all the intestinal walls, to cause stricture, and not uncommonly tend to cause adhesions to the adjacent bowel and produce fistulous formation.

A S Jackson⁶⁶ divides the course of regional ileitis into four phases (1)

there may be loss of blood with resultant anemia, as well as malaise, fever and loss of weight (3) The ulcerative phase is followed by a stenotic process. As a result of the extreme thickening of the intestinal wall, the lumen of the intestine gradually becomes constricted, leading to signs and symptoms of partial intestinal obstruction (4) In the last stage of regional enteritis, multiple fistulas de-



Fig. 42—String sign in terminal ileum. (Dr. Arnold S. Jackson. Regional Enteritis, in Surgery, Gynecology and Obstetrics, July 1937.)

Symptoms at first are suggestive of acute intra-abdominal inflammation and especially appendicitis (2) The symptoms of the second phase of the disease may simulate those of ulcerative colitis, with attacks of diarrhea and crampy abdominal pain. These cases may go unrecognized for months or years, all the while large amounts of bismuth and bland foods being consumed. In some cases

velop that may open either internally or externally through the abdominal wall

Etiologically, there is as yet no final agreement. The first query always is "Are you sure it is not tuberculosis?" To the best of knowledge, this particular lesion is not tuberculosis. Repeated sections have been stained for the tubercle bacillus and in several of the authors' cases, as well as those reported by others,

guinea pigs have been inoculated but there has not been any evidence of tuberculosis

Clinically, ulcerative colitis and regional enteritis are similar. In both, there is usually the history of early exacerbations and remissions. As time goes on, the disease becomes more continuous and more resistant to treatment

Pemberton and Brown have seen both the acute and chronic stages of inflammation of the small bowel. In some cases the appendix was chronically inand ulcers of Meckel's diverticulum reported previously

Adhering to rigid selections, this report comprises 39 cases observed at the clinic from 1922 to date. The presence of the lesion was established by operation or necropsy. Thirty-six patients were subjected to operation at the clinic and two were operated upon elsewhere. One patient died without being subjected to operation.

The age distribution parallels that found in a series of cases of ulcerative



Fig. 43—Regional enteritis showing enlarged mesenteric glands and hose-like thickening of the last eight inches of the fleum. (Courtesv. Surg. Gynec. and Obst., July, 1937.)

flamed, and in others it was acutely inflamed. Appendicectomy was the only operation performed in these cases

The authors have selected only the cases in which lesions originated in the small intestine and were not associated with true ulcerative colitis or with primary granuloma of the cecum. Whenever there has been doubt as to the presence of intestinal tuberculosis, even though the positive evidence was very scanty, such a case has been omitted from this study. Likewise, the authors have not included that small but most interesting group of solitary iteal ulcers.

colitis, in which 29 of the 39 patients were less than 40 years of age. This probably is merely indicative that the more active lymphoid tissue of young people is an important predisposing factor in any inflammatory disease. The sex factor was not significant in the cases of regional ileitis as 23 of the patients were males and 16 were females

In the three cases in which the jejunum only was involved, the involvement was extensive. The ileum was involved in 34 cases. There were two cases of multiple involvement or "skip areas" throughout much of the small bowel



Case 1. Greatly thickened and indurated terminal ileum with involvement of incenteric glands.

7.

Case 3 Regional enteritis involving two segments of the ileum Note the enlarged mesenteric glands



Case 1

Grossly the lesion consists of an inflammatory process which is rather sharply localized to a single segment of bowel, but occasionally involves two or more segments that apparently are separated by intervening segments of normal bowel In the more active phase the involved segment is greatly swollen, In the more heavy, and reddened chronic phase of the disease, marked edema, engorgement, and exudate have disappeared to a large degree, but the intestinal wall is still greatly thickened It feels leathery and in most instances is free of adhesions

Symptoms—Pain, which is the outstanding feature of the disease, was present in 38 of the 39 cases Efforts to localize the lesion by the distribution of the pain are helpful in only one respect, that is, the pain is more likely to be situated below the umbilicus than above it

Fever, which often was associated with chills, occurred in 21 cases and no doubt occurred in others. Secondary anemia occurred in 17 cases. In one case in this series, tarry stools were associated with the attacks of pain and tever.

In this series of cases nausea and voiniting frequently were associated with the attack, and in many instances they had led to an unsuccessful operation. There were no significant changes in the blood, although a macrocytosis was noted in some cases, but this could be considered only a suggestive sign.

A typical, pathognomonic clinical syndrome of regional enteritis has not been elaborated, in fact, the clinical diagnosis remains conjectural or tentative until roentgenological evidence of the disease is adduced

The fact that 26 of these 39 patients had undergone one and often more unsuccessful operations for this disease is

evidence of its seriousness, as is the fact that in the past the disease has remained unrecognized even after laparotomy.

B B. Crohn⁶⁷ states that in the acute type of ileitis the prognosis is altered by the severity and the rapidity of the course of the disease Palliative attempts at drainage, appendectomy or skilful neglect seem useless. Many surgeons have attempted to relieve or cure the disease by anastomosing proximal healthy ileum to healthy colon, thus shortcircuiting the lesion and rerouting the intestinal content over normal mucosa It appears that palliation is not only futile but in addition increases the the risk of subsequent operation That short-circuiting frequently fails, there is no doubt, that it may also times suffice to cure must remain an open question for the time Seventeen cases of ileitis in which no direct operative intervention had been practiced are now under observation (from one to three years) Three patients died of peritonitis and exhaustion. In another patient not operated on, the ileum had to be resected after two years because of a rapidly downhill course with fever. diarrhea, mass formation and obstruc-Four of these patients without operation are seemingly doing well, gaining slightly in weight and showing an occasional slight tendency to diarrhea but no real abdominal distress and no loss of efficiency The author believes that in these patients fistulas will eventually form, or obstruction may take place, though it may take years. And yet, scientific precision and clear thinking require one to maintain the premise that a complete restoration ad integrum is within the possibilities of nature Another four patients are obviously not improving, the symptoms of mild bouts of diarrhea and cramps continue, associated with fluctuating slight loss or

slight gain of weight. The remaining patients are lost to the present follow-up. In short, in the best of hands the prognosis is excellent when a radical resection is performed. Palliative short-circuiting procedures, as well as skilful neglect and so-called conservative medical treatment are still on trial, and the prognosis is still to be determined.

Treatment — The treatment of regional ileitis is essentially surgical and usually necessitates removal of the diseased segment with re-establishment of the continuity of the intestinal tract. The operation may be performed in one or two stages. In a large proportion of the cases the disease is complicated by obstruction, by acute or subacute inflammatory changes, or by the presence of abscesses or intestinal fistulas when the patients are seen by a surgeon

Although six of the eight patients mentioned by Pemberton and Brown who were subjected only to the first stage of the procedure, ileocolostomy, for localized enteritis reported that they were well and free of symptoms for from two to five years after operation, the authors believe that resection of the involved portion of the bowel is indicated in all cases in order to prevent the spread of the infection. In one case in which the patient delayed returning for the second stage, resection, for four years, a recurrence of the process was discovered in a short localized segment of ileum at the site of the previous end-to-side ileocolostomy

The authors think that the interval between the stages of the procedure should be varied, and should depend chiefly on the general condition of the patient and the nature of the complicating lesion. In no instance have the authors seen any progress of the disease occur between the first and second stages when the interval did not exceed six

months, but on the contrary there has been without exception a very marked subsidence of the inflammation which greatly facilitated resection.

Surgical treatment was employed in 36 cases Data are available in 35 of the 36 cases in which operation was performed Twenty-two patients are apparently well, one is in fair health, and six are not well. Two deaths occurred in the hospital, and four patients died after they returned home. The immediate surgical mortality was two or 55 per cent. In these 36 cases, 47 major surgical procedures were carried out with a mortality of 42 per cent.

In three cases in which only a short-circuiting operation was performed, a deficiency syndrome with the hematological picture of primary anemia has developed. It is impossible to say whether or not this syndrome is related to the ileitis. All of the deficiencies are being controlled by liver. In another case a deficiency disturbance, comparable to the wet type of beriberi, developed after the operation. This disturbance cleared up promptly as a result of a normal diet plus vitamin. B

To put the diseased colon at rest and to irrigate and cleanse it, A A Berg⁶⁸ has carried out the following procedure in five cases A left-sided transrectus incision is made extending three or four inches (76 or 101 cm) upward from the symphysis, the terminal ileum is identified and delivered out of the wound The healthy sigmoid is similarly delivered into the abdominal wound healthy ileum, as near to the ileocecal valve as is possible, is cut completely across and its mesentery is divided Both ends are closed by two or three tiers of sutures, an inner chromic catgut suture is made through all the coats, reinforced by one or two layers of interrupted linen or chromic catgut sutures

proximal end of the ileum is joined to the lower sigmoid just above the peritoneal reflection by a side-to-side anastomosis. Several inches above this sideto-side anastomosis the sigmoid is cut completely across, the distal end is closed by a row of chromic catgut sutures reinforced by one or two layers of linen or catgut, and the proximal end is tied off with a heavy silk suture, thoroughly phenolized and brought out through the upper angle of the wound The rest of the abdominal wound is closed in layers The heavy silk suture around the proximal end of the sigmoid is left in situ for from 48 to 72 hours and then removed, leaving a fistula in the proximal end of the sigmoid fecal stream is thus entirely diverted into the lower-most sigmoid and rectuni, and the fistula in the sigmoid permits the free drainage of the products of inflammation from the diseased colon After from 10 to 14 days the colon is irrigated through the sigmoid fistula The entire colon and the diseased portion of the ileum have been removed subsequently in two cases

Tumors

Angiomas of the digestive tract were first observed by Rokitansky in 1855, but few systematic studies have been made of them up to the present time

According to M Brulé, P Hillemand, and J M Génestoux 19 such tumors may be localized in one segment of the digestive tract or distributed throughout its length. In either case the lesions may be circumscribed or diffuse. The circumscribed lesions are sessile or pedunculated red or bluish masses, whereas the diffuse lesions are placques of vascular channels similar to the portwine stains that occur in the skin Whether located in the stomach or intestine, either form may be submucous

or subserous or may infiltrate the entire wall of the viscus

The neoplasms are also of a pseudoulcerative or a pseudoneoplastic type Those of the pseudoulcerative type occur in the stomach, where they cause symptoms of peptic ulcer Thirteen cases of such angiomas have been reported in the literature Angiomas of the pseudoneoplastic type occur in either the stomach or large bowel and may suggest carcinoma

Symptoms—Hemorrhage and anemia may be the only symptoms. When the hemorrhages begin in childhood, a special type of infantilism results. Pernicious anemia may be closely imitated even to the megaloblastic reaction in the blood.

Occasionally acute intestinal obstruction occurs as the result of intussusception, volvulus, or encroachment of the tumor on the lumen

In some cases the angiomas are entirely latent so far as symptoms are concerned

When the origin of any of the described syndromes is obscure, the presence of external angiomas may suggest the correct diagnosis. A definite diagnosis can be made only by endoscopy or exploratory laparotomy

The *prognosis* is grave, 60 per cent of the patients dying of chronic anemia or acute hemorrhage

In most cases the *treatment* indicated is *surgical* since methods such as cryotherapy and diathermy are dangerous in the digestive tract. However, when the angiomas are situated favorably, *sclerosing injections* may be employed and *irradiation* is occasionally found to be effective.

A contribution to the study of Pick's intestinal inelanosis based on two cases of primary melanoblastocytoma is outlined by C. Manzini 70. The patients

were women 42 and 55 years old, and the tumors were situated, respectively, in the small intestine and the descending colon. Minute examination at autopsy excluded the presence of foci of pigmented tissue from which the neoplasms could have originated

Manzini believes that primary melanomas of the intestine arise from the areas of undifferentiated melanoblasts in the subserous laver described by Pick and Brahn in 1935 These areas, which probably represent the remains of the pericelomatic pigment system, do not become visible macroscopically until the fourth decade of life, but can be detected microscopically much earlier The melanin is produced from aromatic groups in the cell proteins under the influence of oxidizing enzymes autopsy on two middle-aged subjects Manzini found such patches, from 3 to 10 mm in diameter, on the visceral peritoneum near the insertion of the mesen-The spots are comparable to the zones of dysembryoplastic melanogenetic tissue in the skin except that they arise under special metabolic conditions in later life when the tissues enter a phase of decreased resistance (Borrel's pig-Resumption of the mentary crisis i pigmentogenetic function always occurs in cells in which this activity has almost disappeared or has remained in abeyance

These findings demonstrate the possibility of a frimary melanoblastoma of the intestine. Additional evidence is the coincidence of the age at which both the pigmented spots and the tumors appear and the frequent location of both at certain definite points along the intestine. The tumors probably arise, not from a single type of cell, but from a system composed of mature melanoblasts, potential melanoblasts, and cells without pigment-producing power. This would account for their polymorphism and ir-

regular pigmentation. Histogenetically they are fundamentally sarcomas derived from undifferentiated mesodermal melanoblasts, but because of their variable histological pictures with no predominating type it is more exact to designate them by the general term "melanocytoblastoma"

Primary melanoblastomas of the intestine are exceedingly rare, only 11 cases, including Manzini's case, having been reported. This fact is explained by the infrequency of melanomas in general, of mesenchymal tumors of the intestine, and of subserous pigmented areas.

Manzini discusses the diagnosis and clinical course of these tumors. He states that, in the absence of other manifestations of abnormal melanosis, the most reliable sign is the presence of melanin in the urine. According to the findings of his researches, the melanin in the tumor appears to be different from that in the normal skin. He discusses also the origin of melanomas in general and the nature and classification of pigment-forming cells.

Carcinoma

E W Rowe and J M Neely⁷¹ report eight cases of tumors of the small intestine, five of adenocarcinoma of the Jejunum, one of colloid carcinoma of the duodenum with possible origin in the pylorus, two of lymphoblastoma, one presenting multiple tumors with the histological appearance of Hodgkin's disease, the other presenting a lymphosarcoma

Symptoms—The symptoms of malignant tumors of the small intestine are vague before the onset of complete obstruction. Early appearance of visible peristals in any part of the abdomen and occult blood in the stool should make one think of tumor of the small

intestine Cases are usually diagnosed by the surgeon as intussusception or obstruction of the intestine, and the true pathologic condition has been revealed either at operation, biopsy or necropsy Intestinal obstruction, intussusception, acute abdomen and exploration of a suspected tumor mass are the common preoperative reasons given for the op-In most cases the roentgen examination, if employed, has consisted of preliminary roentgenography or a routine gastrointestinal examination, not timed for the special observation of the small intestine Certain conditions and drugs must be understood or they com-Hyperthyroidism plicate the picture causes increased motility Mvxedema causes slowness and slowed evacuation Inanition delays evacuation Loss of consciousness stops all movements Atropine slows all movements Fat delays grosser movements, and achylia increases motil-The roentgen examination of the ıtν small intestine, properly carried out, consumes time and is a relatively expensive procedure. In properly selected cases it will disclose the solution to an otherwise puzzling problem Clinicians are recognizing more and more the value ot a careful examination in obscure lesions of the gastrointestinal tract Positive changes depend on the stage of the disease They are not always infallible, and because of the lateness of an opportunity to study the usual case, the observations may not be very determinate Even positive signs may not be pathognomonic, nor does a negative examination exclude the possibility of a tumor There must be careful and intelligent correlation of the clinical observations with the objectives of the roentgen examination Study of the small intestine should begin when the stomach first begins to empty After the examination of the stomach, further observation of

the small intestine should be made at intervals of half an hour—at six hours for ileum, at nine hours for the ileac stasis and again at 24 hours for occasional ileac stasis. Ileac stasis, or gas, in the small intestine always needs explanation. A barium sulfate enema should be employed not only for colon but also for a complete ileac study. Sometimes the contrast enema is an advantage.

C W. Mayo and W S Nettrour⁷² state that carcinoma of the small intestine is infrequent and comprises 0.47 per cent of carcinomas of the gastrointestinal tract The jejunum is the most common site for carcinoma of the small intestine, and carcinoma of this region represents 015 per cent of all gastrointestinal carcinomas The symptoms are those of intestinal obstruction with progressive anemia. Cramps and epigastric discomfort are commonly the chief symptoms Cramps usually occur three or four hours after eating "Gas," "rumbling," and "bloating" are common Weakness, fatigability and anemia often precede the gastrointestinal symptoms Occult blood in the stool is an important finding

The prognosis is unsatisfactory. The operative mortality is 20 per cent, while the average duration of life is 176 months following operation. Although the patients lived only a short time the relief of obstruction and the comfort of the patients seemed to justify the surgical procedures. Perhaps the digestive activity of the jejunum, the abundant supply of lymph, and the high grade of malignancy are important factors in the gravity of the prognosis.

Treatment—Resection and enteroanastomosis were the procedures of choice and could be performed in 15 (48 per cent) of the cases. Of the palliative surgical procedures, enteroanastomosis was performed in 11 (35)

per cent) of the cases, while gastroenterostomy was performed in only two cases. In two cases the abdomen was closed after an exploratory laparotomy, and in one case no surgical treatment was given A detailed description of the surgical technic has been reported previously by Mayo cated as an excellent substitute for peritoneum, but if the raw surfaces are multiple in number, and particularly in the pelvis, the end result is not always satisfactory owing to the restriction of both gastric and intestinal motility

Ammoniotic fluid has been tried for the reduction of adhesions, but the re-



Fig. 44—Obstruction in the jejunum which was interpreted as carcinoma (Case 29). (Drs. Chrs. W. Mixo and Walter Scott Nettrour. Carcinoma of the Jejunum, in Surgery, Gynecology and Obstetrics. Sept., 1937.)

Plication of the small intestine as prophylaxis against adhesions is advocated by T B Noble, Jr 7.3 Loss of peritoneal surface of intestines is a frequent complication of a pathological or traumatic process in the abdomen. If the denuded area is left uncovered or improperly treated, adhesions develop which may lead to more serious consequences such as intestinal obstruction, etc. The omentum has long been advo-

sults appear to throw much doubt upon the value of introducing large volumes of such a foreign fluid. Digestive ferments such as *papain* and *pepsin* have also been employed, but this subject is apparently still in its experimental stage

In many abdominal operations, the author has used a simple procedure to obviate the development of adhesions. The principle is to bring the raw surfaces of adjacent segments of small in-

testines into apposition and suture them Since the procedure has been used in a wide variety of cases simplification of description is offered so that the principle is better shown. Three degrees of procedure are therefore described chromic No 00 catgut is started at the root of the mesentery and carried up to the mesenteric margins of its bowel, approximating the mesentery as shown in Fig 45 The same suture is continued now at right angles along the mesenteric

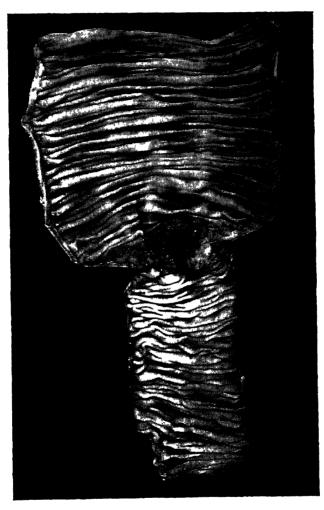


Fig 45—Carcinoma of jejunum (Case 29) (Drs Chas W Mavo and Walter Scott Nettrour Carcinoma of the Jejunum, in Surgery, Gynecology and Obstetrics, Sept., 1937)

1 There is a single rough, denuded or raw spot on the intestinal wall after dissection of the adherent bowel to free it from some pathologic process. The loop containing the damaged area is folded so that the denuded surface is covered by the peritoneum of the adjacent wing of the fold. A running

margin of its bowel to the angle of the fold, running around the denuded area as seems best fitted to cover it

2 There are several damaged areas After carefully freeing the bowel and mesentery a fold is made as will best cover most raw areas, which usually occur on the same surface. The length





Fig 46—Case of complete obstruction lasting four days due to strangulated herma Dilated and collapsed bowel shown (Courtes), Am J Surg, Jan, 1937)

Fig 47—Loop of bowel proximal and distal to area of incarceration, collapsed gut filling with gas. Plication done to prevent completion of tendency toward intussusception. Photograph shows beginning of mesenteric suture and lines up mesentery to bowel which are to be sutured together (Courtesy, Am. J. Surg., Jan., 1937.)



Fig 48—Mesenteric approximation completed Mesenteric margin of the bowel being sutured, the end of the suture to be at a point under the left thumb in the illustration. The area of incarceration just to the right of the thumb, therefore, is not at the point of angulation. (Courtest, Am J. Surg., Jan., 1937.)

Fig 49—Completion of plication viewed from above Mesenteric suture not visible, being vertical up mesentery to bowel margin. Filling of collapsed bowel well under way through normal peristalsis. Convalescence was uneventful. (Courtesy, Am. J. Surg., Jan., 1937.)

of the mesentery will determine the length of the wing of a fold Ordinarily a wing is from three to four inches long, making each plication include six or eight inches of bowel. In some cases the mesentery is long enough to allow wings of eight inches, or a loop plicating 16 inches in all. The plication suture is always be-

3 In the presence of very extensive inflammation with marked peritoneal damage, a more radical type of plication is used. If a single plication cannot cover all the raw areas, other plications may be added so that in place of two wings closely approximated by suture there may be three, four, or as many more

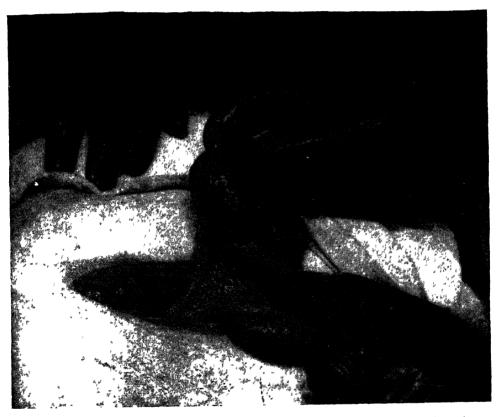


Fig 50—Completed plication viewed from side, showing mesenteric stiffening through suture shown in Fig 47 Area of threatened intussusception just distal to area of incarceration shown (Courtesy, Am J Surg., Jan., 1937)

gun at the root of the mesentery and then continued at right angles along the bowel as seems best. Since the lumen is not constricted by this method, a raw area on the surface of the bowel opposite the mesenteric attachment may be covered with any part of the surface of the opposite wing of the plication. Furthermore, by inspection, no inhibition of intestinal movements ever occurred from such intentional folding.

as needed, each suture to each wing beginning at the root of the mesentery. When this becomes necessary, the entire length of the small intestines may be plicated. It is in this respect that the folded mesentery and intestines resemble a closed fan

The illustrations show the plication of one loop of bowel and are chosen for clarity and ease of demonstration of the operative steps

During the past ten years several hundred cases were treated with intestinal plication. None have developed any symptoms of adhesions.

Technic — New Methods of Intestinal Anastomosis — F Glenn⁷⁴ de-

51) is used in the following manner A snare is placed at each extremity of the segment of bowel to be resected after the mesentery has been divided and the blood vessels ligated. By means of set-screws, the snares are tightened

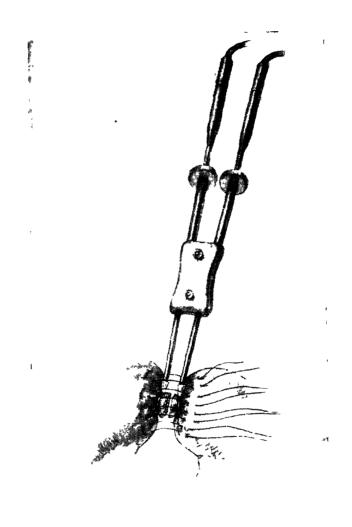


Fig 51—The instrument is shown after the resection of a segment of bowel, with the stumps held in alinement. The bakelite tubes through which the snares operate are in position in the special crossbar clamp. (Courtes), Am. J. Surg., June, 1937.)

scribes an instrument which consists of two wire snares with attachments to a Bovie unit. The snares operate through bakelite tubes which can be held in close alinement in a specially constructed crossbar clamp. The instrument (Fig. until they obliterate the lumen of the intestine. Using the cautery, the intestine is divided close to the snares and removed with its mesentery. The stumps of bowel held in the snares are now brought into alinement by approximating

the bakelite tubes and are secured in this position by fitting the tubes into the crossbar clamp. The divided ends of bowel are brought together with mattress sutures, one of which is placed so that it embraces the snares. Beginning with those closest to the mesentery, all sutures are tied with the exception of the one embracing the snares. The domen is closed in the routine manner

The experimental work of the author in devising this method seeks to avoid trauma to the intestinal wall, contamination of the field of operation.

A new clamp to aid in intestinal anastomosis has been devised by H. B. Stone 75 The instrument has proved useful for end-to-end, end-to-side, and

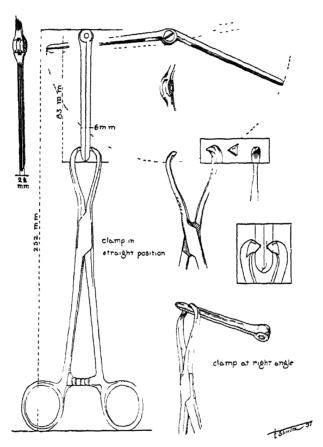


Fig 52—Details of the clamp, with dimensions and positions (Dr Harvey B Stone Method of Intestinal Anastomosis with a New Clamp, in Surgery, Gynecology and Obstetrics, Sept , 1937)

connection with the Bovie unit is made now and the current through the snares cuts cleanly through the inverted stumps of bowel, leaving within the lumen a very small amount of untraumatized intestinal wall. The instrument is now discarded and the last mattress suture tied. Reinforcing sutures are placed between the mattress sutures and the ab-

side-to-side types of operations. The clamp is used in a so-called aseptic type of suturing, the general principles of which have been developed in the Parker-Kerr and various other procedures.

The technic, for instance of end-toend suture, is as follows. The gut is crushed across at the desired levels by

crushing clamps leaving a groove. The hinged jaw piece of the clamp herewith described is placed across the gut at the crushed groove and solidly locked in place by setting the handle-piece firmly into the sockets in the tips of the jaw piece. The portion of gut to be removed is cut away with the cautery close against

The ends of this posterior suture are tied. Now the clamps are rotated toward each other and a similar suture unites the gut walls in front of the clamps, but in this suture the ends are not tied but left loose so that the stitch may be drawn taut after the clamps are removed. The compressing handles are



Fig 53—Manner of placing clamps on bowel before resection of gut (Dr Harvey B Stone Method of Intestinal Anastomosis with a New Clamp in Surgery, Gynecology and Obstetrics, Sept. 1937)

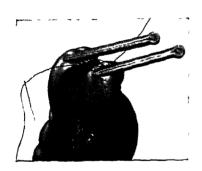


Fig 54—(aut resected Ends to be anastomosed brought side by side Posterior continuous suture being placed behind clamps. Fixation handles omitted from sketch for simplicity. The two ends of this suture are to be tied. (Dr. Harvey B. Stone, Method of Intestinal Anastomosis with a New Clamp, in Surgery Gynecology and Obstetrics, Sept., 1937.)

the anastomosis clamp. The same process is applied to the other end of the gut to be resected, and the ends to be anastomosed, held firmly by the special clamps, are brought closely together, end-to-end. A continuous suture of median silk unites the gut walls of each end behind the clamps, which are rotated slightly away from each other during the placing of the suture.

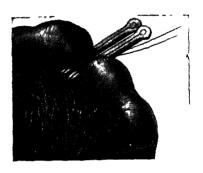


Fig 55—Anterior suture being placed over clamp blades Handles omitted for simplicity (Dr Harvey B Stone Method of Intestinal Anastomosis with a New Clamp, in Surgery, Gynecology and Obstetrics, Sept , 1937)

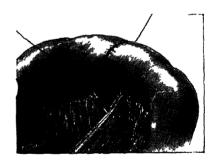


Fig 56—Clamps withdrawn Anterior suture pulled snug, closing anastomosis Ends of anterior and posterior sutures tied together (Dr Harvey B Stone Method of Intestinal Anastomosis with a New Clamp, in Surgery, Gynecology and Obstetrics, Sept 1937)

now released from the tip of the hinged jaws and set on the hinged joint end instead. By gentle pulling the jaws are withdrawn from between the rows of sutures, front and back, the front row being pulled taut as the jaws of the clamps are slipped out. The corresponding ends of the front and back sutures are tied together and the anastomosis is accomplished. It can be further sup-

ported by an additional row of mattress or continuous sutures if so desired.

The squared holes and points of the 1aw and handle pieces permit the assembled clamp to take three forms Taw and handle may be set together in the same long axis so that they form a straight line with each other, or they may be clamped together with the handle and blade at right angles to each other, the angle being directed either to the right or left of the surgeon as he may elect. In certain positions this has considerable advantage For instance, several anterior resections of growths rather low in the sigmoid have been done with these The clamps on the stump of clamps gut are put on with jaws and handle at right angles to each other, which permits manipulation in the confined space of the pelvis that would be impossible without this feature

In summary, the clamp possesses firmness and security for use in the "aseptic" type of anastomosis by applying compressive power to the tips of the blades, and also has adaptability because it may be employed as a straight or right angle clamp

LIVER

Laparoscopy

H Kalk⁷⁶ discusses his method of laparoscopy (originated by Jacobaeus in 1913), gives the indications for its use, and reports his diagnostic and operative (puncture of the gall bladder and cutting of the strands of adhesion) results during the past 12 years. He stresses the advancements that have been made which make it possible to determine whether surgical treatment is suitable in a number of diseases. Up to this time these determinations had not been possible by other means. He assumes that the tech-

nic and instrumentation are already well known.

Contraindications to laparoscopy are active inflammatory processes and powerful adhesions within the abdomen. By means of laparoscopy almost the same observations may be made as when the anterior wall of the abdominal cavity of a cadaver is removed; especially enlargements, reductions, locations, and displacements of the individual organs, tumors, and their metastases may be seen The author cites numerous examples of how a tensely filled gall bladder exerts pressure or perforates, and how it retracts. in cases in which functional disturbances of the liver have already been determined by other diagnostic means The various types of hepatic shrinkage, as to form, surface markings, and color, may be distinguished easily by laparoscopy, and in polyserositis the adhesive pericarditis may be recognized Single tumors, as for example, primary carcinoma in a cirrhotic liver, may be recognized only by this method, and the origin of tumors which can be detected externally by palpation may be studied, and indications for their surgical management may be observed In jaundice the color of the liver varies from yellow (simple jaundice) to green (occlusive forms of jaundice) Gallstones can be located Paracentesis through the liver of the tensely filled gall bladder causes amelioration of the symptoms In inflammatory conditions of the gall bladder or when stones are present roentgen examination and sounding will usually be sufficient for diagnosis. When the condition is correctly diagnosed the best results from treatment will be obtained

Amebic Abscess

Twenty-five cases of amebic abscess of the liver among the last 34,944 ad-

missions, have been studied by J R Young and L J. Bristow 77 Of the patients admitted for primary pathologic changes of the liver, 37 per cent, or one in three, had amebic abscess history suggestive of amebiasis was obtained in only 13 patients, and only six had a diarrhea on admission to the hos-The relatively high incidence of persons who have an amebic abscess of the liver with no antecedent history of a dysentery is explained by the fact that slight amebic infections limited to the right half of the intestine may not produce diarrhea, while the same degree of infection in the left half may produce symptoms, and the nearer the rectum is approached by the infection, the more pronounced are symptoms produced Only five patients had received emetine previous to the present illness. If used oftener, amebic abscesses would be less frequent

Symptoms—From the histories, as nearly as could be determined, the average duration of symptoms was more than 21 weeks, the extremes being 18 months for the longest and two weeks for the shortest In reviewing the symptoms as presented, pain and/or tenderness in the region of the liver and fever occurred in all cases Pain in the upper right quadrant associated with an enlarged, tender liver and a sallow, muddy skin should make one suspicious of amebic hepatitis, whether or not the patient gives a history of a past diarrhea other most frequently noted symptoms were loss of weight and vomiting in 15 cases, chills in 13 and sweats in ten while seven patients gave the history of having pain in the right shoulder All the patients had a secondary anemia Stool examinations are helpful only when positive, and a negative stool by no means rules out amebiasis Roentgenoscopy is one of the most important and reliable diagnostic aids, especially fluoroscopy, where elevation and fixation of the right leaf of the diaphragm is a constant occurrence.

Treatment—The treatment of amebic abscess of the liver consists of specific therapy, closed drainage (aspiration), open drainage, or a combination of these methods. As soon as the diagnosis is made or suspected, 1 grain (0065 Gm) of emetine daily for from six to ten days is given If the patient is not relieved, the abscess should be emptied by aspiration. If aspiration is not done or is not successful, open drainage of the abscess by the transpleural or abdominal approach is indicated, depending on where the abscess is "pointing" No matter what method of drainage is used, emetine should be given to every patient having abscess of the liver

Portal Thrombosis

Thrombosis of the portal venous system is discussed by E C Pallette⁷⁸ from the standpoint of etiology, symptomatology, frequency, pathologic physiology and treatment The condition is too infrequently recognized as a clinical entity The acute condition may closely simulate an abdominal emergency, and in the chronic form the associated splenomegaly should not be regarded as successfully amenable to surgical treatment Unfortunately there is no treatment of any essential value in this condition. In acute cases the usual procedures for the treatment of shock, ileus and the like In his own case the are instituted author felt that perhaps the repeated injections of intraspinal procaine hydrochloride given in the hope of relieving the marked ileus present was of considerable value and perhaps definitely influenced the outcome toward recovery The basis for this opinion is that, in relieving the critical distention of involved intestine, the already embarrassed circulation to that loop is relieved. The huge ascites can be controlled by paracentesis. In the chronic cases, instructions should be given as to the avoidance of all alcoholic beverages or of any drug toxic in any way to the liver.

On the basis of the nature of chronic occlusion of the portal vein, J P. Simonds⁷⁹ divides the 94 reviewed cases into two groups. In one group the vein was reduced to a fibrous cord with relatively slight canalization. In the other, it had been replaced by an elongated mass of spongy, cavernous tissue in which traces of the wall of the vein were usually, though not always, discernible The majority of those who have studied this condition believe that it is merely the result of organization of a thrombus with marked recanalization Others consider the lesion a congenital malformation Pick expressed the opinion that the condition is a neoplasm—an angioma or cavernoma of the hepatoduodenal ligament

The most constant accompaniment of chronic occlusion or stenosis of the portal vein is enlargement of the spleen Changes in the liver are not so extensive or so frequent as might be supposed

In five of the reviewed cases splenectomy was performed One of the patients subjected to this operation survived for seven years The infrequency with which the spleen is removed in this condition is surprising as splenectomy would seem to be the logical treatment. It reduces the burden on the collateral circulation usually by about one-fifth, and when the spleen is greatly enlarged, probably When the collateral circulation has become so incompetent that rapidly increasing ascites develops or when the esophageal varices have become so large as to be the source of frequent and copious hemorrhage the patient will

survive for a period of from only a few months to two or three years

Enterectomy in Hepatic Cirrhosis or Portal Obstruction with Ascites-A case of portal cirrhosis with ascites, is cited by M K. Fuller, D D. M Cook, O. M. Walter, and N. Zbitnoff⁸⁰ with a duration of more than 22 months treated by tapping, with no tendency toward diminution After massive intestinal resection (enterectomy) the rate of ascitic accumulation was immediately approximately halved, and following a period of a gradual decrease of the ascitic fluid its formation ceased nine months after the operation The patient has now been free from ascitic fluid for 29 months After operation the patient was permitted to follow his appetite as to any type and amount of food and liquid desired His output of urine has averaged 1300 cc daily Though the patient has not suffered from constipation, he has had no tendency to diarrhea, which is sometimes noted following massive enterectomy

Talma Operation—The object of the Talma operation is to produce artificial adhesions of the omentum and spleen to the anterior abdominal wall and thus provide a collateral route for the blood which otherwise would go to the liver This is done to prevent congestion in the region of the liver O Henningsen 1 points out that the operation is performed especially in cases of atrophic cirrhosis of the liver although it is still unknown whether the ascites is due to stasis alone or whether toxic or infectious influences also play an important part in its occurrence The operation is performed also in cases of biliary cirrhosis, cardiac cirrhosis, and Curschmann's disease, even in cases of ascites due to cardiac insufficiency When there is icterus indicating injury of the liver the prognosis is unfavorable. The opera-

tion is contraindicated also by vitium cords with generalized hydrops only suitable cases are those in which there is interference with the portal circulation due to destruction of the central veins, i ϵ , cases of isolated portal stasis The course of this condition is long It is not only until late that the chronic intoxication is manifested by ascites and bleeding from the digestive tract, particularly the esophagus (evidence of congestion in the region of the portal vein) After the appearance of these congestive phenomena the condition usually progresses very rapidly The congestion can be relieved by the opening of new collateral channels The functional state of the liver is also of importance. Icterus and acholia, xanthoma and pigmentation of the skin, and urobilinuria necessitate caution. With the beginning of icterus the prognosis rapidly becomes worse

In an attempt to clear up this problem the author carried out experiments on animals. It is well known that experimental animals soon die when the portal vein is ligated before its entry into the liver. In experiments on 15 rats the author sutured the omentum intraperitoneally to the peritoneum over a large surface and placed the spleen in a makket of the omentum. Ten days later he ligated the portal vein and severed it at the porta hepatis. The operation was well tolerated by all except one rat The animals presented no differences from normal animals. However, it as possible that some of the blood reached the liver in spite of the developing collateral channels The experiments prove merely that the portal circulation can be replaced by collateral channels by a procedure similar to the Talma operation It is necessary only that the number of newly formed vascular anastomoses be large

Indications - Spontaneous bleeding from the stomach and intestinal tract 15 an absolute indication for the operation, whether ascites is present or not When severe hemorrhages occur from ruptured esophageal varices it is necessary, of course, to delay the operation to see if the patient will recover from the effects of the bleeding The procedure must be very conservative A small midline incision under local anesthesia is sufficient for either intraperitoneal or extraperitoneal fixation of the omentum When the spleen is greatly enlarged a portion of the omentum should be sutured to its surface. In extraperitoneal fixation, abdominal hernia usually doesn't play an important rôle The author disapproves of the suturing of loops of intestine together or of additional drainage of the abdominal cavity from the pouch of Douglas He states that when the operation is performed in the presence of the indications cited and in the manner described the dangers are very slight Therefore too much conservatism in the selection of cases is to be avoided By the described treatment, life can be prolonged and made more bearable for a period ranging from months to years

Lithiasis of the Intrahepatic Bile Ducts

P Santy and P Malley-Guy⁸² discuss the clinical aspect of lithiasis of the intrahepatic bile ducts on the basis of some cases of their own and a study of 25 cases collected by their student, Sorlin, in his thesis Intrahepatic biliary calculi are of importance chiefly because they may be responsible for the failure of well-planned complete operations on the extrahepatic bile ducts

Such calculi may be scattered throughout the bile ducts, involving all of the liver parenchyma, or localized in one or more branches of the intrahepatic bile ducts, involving only one lobe Of Sorlin's 25 cases, 13 were of the diffuse type and 12 of the localized type.

In the majority of cases the calculi are discovered at autopsy on patients who have been operated for biliary duct disease or who have shown symptoms of such disease for a long time Occasionally they have been found in patients who were operated on because of symptoms of gastric perforation, subphrenic abscess, or abscess of the liver. At operation on the gall bladder and bile ducts, an intrahepatic biliary calculus is rarely found in one of the first branches of the hepatic duct even if this duct and its bifurcation are explored

The authors have found that ordinary roentgenography rarely reveals the presence of intrahepatic biliary calculi. If an opaque area is shown in the liver area it is difficult to determine whether it is a calculus or an area of calcification in the liver parenchyma. On the other hand, roentgenography after the injection of lipiodol into the bile ducts shows clear areas in the opaque medium if intrahepatic stones are present. Such a roentgenographic study may be made in the course of, or soon after, operations on the biliary tract.

In cases with numerous calculi scattered throughout the intrahepatic biliary ducts, which have resulted in the destruction of large areas of the liver parenchyma, the condition is fatal and operation is not indicated. In cases of localized intrahepatic calculi, removal by hepatotomy is possible. For this operation, the authors advise the use of the electric cutting current While the stones may be located by palpation of the liver, they prefer roentgenographic study with the injection of lipiodol at the time of the primary operation for gallstones or for stones in the common duct A single roentgenogram suffices

"Liver Death"

On the basis of previous clinical and experimental evidence which has been reported by F F. Boyce and E M. McFetridge⁸³ the following theory to explain the occurrence of this "liver death" or "liver-kidney syndrome" has been evolved

- 1 The same syndrome is apparent and the same underlying factors are operative in the various conditions studied (post-operative biliary disease, postoperative pancreatic disease, and hepatic trauma), and, on the basis of a casual survey of unselected autopsy reports in cases of disease of the thyroid gland, burns, and intestinal obstruction, it appears that this same syndrome may develop in these and perhaps other pathological states in which it has not yet been identified.
- 2 The underlying factor is hepatic damage of some degree either present previously or produced by direct trauma.
- 3 When such a strain is superimposed on the existing hepatic disability, the damaged liver cells, failing in their function, release into the circulation some potent toxic substance which, on the basis of experimental evidence, seems to be water soluble
- 4 This substance, circulating in the blood, is excreted by the kidneys through the convoluted tubules, and they, unfitted by nature for such a load, promptly break under it
- 5 The two types of liver death originally described by Heyd are a single pathological process Cases in which sudden death occurs with hyperpyrexia and only hepatic changes are apparent at autopsy represent the first stage of the process which terminates in deferred death from uremia, in which renal as well as hepatic changes are apparent at autopsy

To prove this theory both positive and negative evidence is necessary. On

the positive side, the toxic substance must be isolated from the damaged liver cells. This the authors are now attempting to do. On the negative side it must be proved that the toxic substance does not originate elsewhere in the biliary system. The authors report experiments carried out by them to establish such proof

According to A S. W Touroff,⁸⁴ numerous cases exhibiting a post-cholecystectomy syndrome consisting of unexplained rapidly rising temperature, pulse, and respiratory rates, associated with shock and vasomotor collapse, and ending in early death, have been reported in the literature

When the existence of postoperative complications such as peritonitis, hemorrhage, pneumonia, embolism, etc, are ruled out clinically and no cause of death is apparent, such a syndrome has been attributed commonly to a condition which has been termed "liver shock"

The diagnosis of "liver shock" in most of the cases reported in the literature was made clinically, and few adequate post-mortem examinations to corroborate the diagnosis appear to have been performed

Of a series of 1360 cholecystectomies reviewed by the author, four cases which exhibited the typical postoperative clinical course of so called "liver shock" with unexplained fatal termination, were subjected to adequate post-mortem study

In each instance, the essential cause of death was found to be unrecognized fulminating intraperitoneal or pulmonary infection, no case of genuine "liver shock" being encountered

In patients, suspected to be suffering from so called "liver shock," it is impossible during life to rule out with certainty the presence of some of the more serious postoperative complications

responsible for the clinical manifestations

Such complications can be excluded only by adequate post-mortem examination

The latter therefore constitutes the only means of corroborating the diagnosis of "liver shock."

Since the vast majority of diagnoses reported in the literature were made in cases which were not subjected to such examination, the former cannot be accepted with finality, and the actual incidence of "liver shock" remains in doubt

The opinion of the author, based on a careful study of a small group of cases, is that genuine "liver shock" is much less common than has been assumed generally

It appears that, in patients suspected to be suffering from "liver shock," unrecognized fulminating infection is the most common cause of the clinical manifestations

All patients exhibiting the syndrome under discussion should be suspected of harboring virulent infection, for which early, extensive, and thorough search should be conducted during life

Infection, if discovered, should be dealt with promptly and vigorously in the hope of occasionally saving the life of a patient whose outlook for recovery otherwise is hopeless

STOMACH

Cardiospasm

The condition was first described by Purton in 1821 as idiopathic dilatation of the esophagus E L Eliason and W H Erb⁸⁵ state that since then various names have been applied to it in an effort to have a descriptive, etiological term Mikulicz popularized the term cardiospasm, postulating the theory that the

obstruction was due to spasm of the cardiac sphincter at the lower end of the esophagus. This has become the generally used term in the literature for the "condition of dilatation and hypertrophy of the esophagus, where on postmortem examination no obstruction to the lumen can be found distally" Phrenospasm, achalasia, esophagectasia, and preventriculosis are synonymous terms

Pathology-The most characteristic pathological change is the huge dilatation of the esophagus. The esophagus may assume one of three characteristic forms, fusiform, flask shaped and sigmoid shaped These are probably degrees of the same process, the sigmoid shaped dilatation being the terminal stage, where the esophagus not only is dilated but has lengthened Always accompanying this huge dilatation there is a commensurate degree of hypertrophy of the muscle wall Occasionally the cardiac sphincter appears to present distinct hypertrophy Such instances are exceedingly rare Because of the fact that definite esophageal obstruction can be demonstrated pathologically they probably should not be classified as cases of cardiospasm in the manner that Walton conceived of this term

In advanced cases, secondary to stagnation of food, an ulceration and quite often an inflammation of the lower end of the esophagus is seen, MacCready reports small white patches of epithelial proliferation or leukoplakia in one specimen Rake also found definite evidence of malignancy in three of 15 fatal cases

Etiology—Many factors have been advanced as etiological agents, with a wide variance of opinion. The experimental work of Knight on cats so clarified the pathological physiology that Eliason and Erb abstracted his conclusions and treated two cases of cardiospasm by re-

section of the sympathetic supply to the cardiac sphincter.

Cardiospasm occurs in individuals of all ages, the youngest being a child of two days reported by Jackson, while Walton reports a case in a woman of 73 years. Aikman reported three cases diagnosed by x-ray studies made on the third, fourth and fifth day of life. The average age is about 40 years. The ratio between females and males is as 3 1, though Sturtevant states that it is more common in males.

Symptoms—The main symptoms are substernal pain, dysphagia, vomiting of undigested food and loss of weight The pain varies in severity from a mild discomfort to an agonizing pain so that in some cases the question of differentiation from a true angina confronts the clinician Vomiting occurs shortly after eating and sometimes before the patient can leave the dinner table No nausea accompanies the vomiting In contradistinction to rigid, organic or cicatricial obstruction, liquids, especially cold ones cause almost as much difficulty in swallowing as solids The weight loss progresses to a certain level and then as a rule the patient is able to maintain his weight at this level The onset is frequently related to some psychic shock, such as the death of a member of the family However, when once manifestations of cardiospasm have developed, there is no tendency to spontaneous remission The condition usually does not rapidly progress to a fatal outcome even if untreated Gould reports a case which after duration of symptoms for 41 years, finally succumbed to manition

Diagnosis—The diagnosis is easily made by x-ray examination which reveals a dilated, elongated and atonic esophagus with the cardiac end of the esophagus constricted to an awl-like point. The diagnosis is confirmed by the

use of the esophagoscope Carcinoma and organic stricture must enter into the differential diagnosis. Cardiospasm, though more uncommon than carcinoma, is not as rare as is generally believed MacMillan, in a statistical study of diseases of the esophagus, found that carcinoma was the cause of 40 per cent of 878 cases of dysphagia, while cardiospasm was the etiological factor in 15 per cent

Treatment—The accepted treatment at present is dilatation of the cardia. Numerous technics have been developed of which the more common are the mercury bougies of Hurst, hydrostatic dilators of Plummer, air dilator of Tucker and gastric tube and dilata-The results tion method of Einhorn of this method of treatment are best given by quoting the series reported from the Mayo Clinic by Moersch in 1932 treated by use of the Plummer dilator Of 810 cases which had been observed, 804 had been treated, 670 patients were traced, 475 were considered cured, including those slight intermittent dysphagia, 105 patients were moderately relieved, 32 were slightly relieved and 32 received no benefit, nine died from splitting of the esophagus, two died from starvation and 12 died at home, cause unknown It is obvious that esophagoscopic manipulation is not the harmless procedure that one usually considers it. This is further supported by the reported mortality of 15 per cent by Mosher in 938 esophago-

Knight's experimental work suggested that improvement would result from sympathetic denervation of the cardia. To effect a denervation in the human, it is necessary to excise the left gastric artery with its surrounding fat and nervous tissue. This was done in five cases with some improvement in all, though in

one in which there was definite hypertrophy of the cardiac sphincter, there was the least amount of improvement This denervation could also be accomplished by a bilateral cervicothoracic ganglionectomy designed to include the upper thoracic ganglia. One such case is reported from the Mayo Clinic with relief of symptoms with, however, the accompanying Horner's syndrome This does not seem warranted in view of the simpler surgical procedure as outlined by Knight

With this résumé of the subject of cardiospasm, two cases are presented which were treated by sympathetic denervation as originated by Knight

Results—Case 1 showed remarkable clinical improvement which could be attributed to the denervation alone. It is true that improvement was mainly clinical and x-ray examination still showed a dilated esophagus though the roent-genologic appearance shows definite improvement in tone. These x-ray findings were duplicated in second case.

Of further interest in the first case was the ease with which the cardia could be explored by invaginating the stomach wall. No attempt at dilatation was made but this probably would be a worthwhile addition to the operative technic

The improvement was not as marked in the second case. Here is emphasized the necessity of close co-operation between the endoscopist and the surgeon Denervation made the dilatation by Dr. Gabriel Tucker easier without which, however, the case would have had to be considered a failure.

Pylorospasm

H Knauer⁸⁶ points out that, because the stimulus threshold of the center of vomiting is rather low in nurslings and small children, every infection, not only a cerebral one, may be accompanied by vomiting Moreover, such attacks may be followed by habitual vomiting. However, if vomiting appears during the first few weeks of life and is especially massive and explosive, pylorospasm or pylorostenosis is usually thought of After pointing out that this condition is comparatively frequent, the author shows that two different terms for the same or at lease extremely similar disease entities indicate that the etiology of the condition has not been completely explained as yet Some apply the term hypertrophic pylorostenosis, while others adhere to the term pylorospasm, some assume an abnormal narrowness of the mucosa, others see the cause of the symptoms in a primary, tumor-like muscular hypertrophy, and still others assume a primary stenosis followed by secondary muscular hypotrophy Still other theories have been advanced and it is possible that the different theories are justified, for the reason that the anatomic foundation may not be the same in all cases The author also cites cases in which the symptoms of pylorospasm are of purely nervous origin. In such cases the vomiting usually ceases as soon as the children are hospitalized, but it often recurs when the children are returned to the nervous parents The author thinks that various factors concur in order to produce the condition, which he designates as "pylorospasm in simultaneous hypertrophic pylorostenosis" He gives several case histories which illustrate the justification of designating the condition as he does He says that for years he was an advocate of the conservative method of treatment, but in view of the fact that of the large number of conservative measures which have been recommended none produce satisfactory results, he now advises surgical treatment for the pylorospasm with hypertrophic stenosis. Of course he does not recommend an immediate operation for every patient who is hospitalized with the diagnosis of pylorospasm. However, if after several days of observation the vomiting does not cease and other symptoms of pylorospasm are present, the operation should be performed for it is not advisable to postpone it for weeks until the child has become extremely weak. It is of course essential that the operation for hypertrophic pylorostenosis be done only by experienced surgeons, the after-treatment should if possible be conducted in the pediatric clinic

Volvulus

Volvulus of the stomach is a great rarity E. Tolboll87 believes his case of torsion about both the longitudinal and the transverse axis in a woman, aged 43, is the first Danish case of total volvulus of the stomach He says that in this disorder there is a change of position of the stomach with a twisting of about 180 degrees about the longitudinal or the transverse axis In partial torsion only part of the stomach turns about the transverse axis, in total torsion there is a turning of fully 180 degrees about the longitudinal axis, which may be complicated by a secondary torsion about the transverse axis The idiopathic form, always total, includes all cases without pathologic changes in the stomach, presumably because only the sound stomach can perform such marked shiftings in localization. In the symptomatic form, always partial, pathologic gastric or perigastric conditions are present. This form, far more frequent than the idiopathic, always affects the pyloric horizontal part of the stomach While the pathologic changes often explain the mechanics of partial torsion, the origin of total volvulus is especially difficult to account for

Gastroptosis and hypermobility are regarded as predisposing factors

Diagnosis-In total volvulus this is difficult in spite of several characteristic signs-violent vomiting, vomited matter never mixed with bile or feculent, rapid cessation of vomiting followed by spitting up of regurgitating mucus from the esophagus, the patient's inability to take a particle of food, development of meterorism localized to the upper left part of the epigastrium and at first limited to this region, remarkably slight tenderness of the epigastric tumor in view of the volence of the disturbance, and finally cardial obstruction making introduction of the stomach sound impossible. The last-named condition is of great significance if the presence of a foreign body in the esophagus is excluded but may fail in the milder cases without torsion about the transverse axis

Treatment- 1s soon as possible, this is surgical. The symptoms in partial volvulus are less pronounced, but there are violent vomiting and intense pain in the epigastrium, which may disappear as suddenly as they set in, when the torsion ceases. Even though the danger passes for the time, omission of intervention is risky, as the prognosis in partial volvulus also is doubtful Roentgen exammation is as important and decisive in partial volvulus, in which the diagnosis is hardly possible without its aid, as it is difficult and uncertain in total volvulus. Thirty-three cases of total volvulus were reported up to 1926 Of the 34 cases, including the author's personal case, necropsy was done in the ten cases in which operation was not performed In six of the remaining cases death followed the operation and in 18 there was recovery Diagnosis was made before operation in five cases Most cases occurred in adults, aged from 40 up, but two cases are recorded in children aged respectively two (Siegel) and five (Dujon) years.

Nonmalignant Pyloric Stenosis

T I. Bennett88 explains the majority of the failures of medical treatment of pyloric stenosis by neglect to meet the requirements and habits of the individual patient There is no other disease in which the personal factor is of more importance, and, if peptic ulcer is not treated more successfully in 1937 than it was in 1927, it is because many physicians and surgeons still continue to adopt a fixed system of treatment, without realizing that, though it may be excellent, it must always require some measure of individual adjustment An extreme illustration of this has been afforded by the transient popularity of the treatment of peptic ulcer by means of injections of histidine Apart from ridiculous forms of treatment such as this, a proper proportion of successes cannot be secured unless each case is judged on its merits and the diet and medicine are arranged in each case so as to secure the measure of gastric rest necessary to bring about permanent healing and health. It is a mistake to assume that organic narrowing of the pyloric canal, even of high degree, must in all cases be treated surgically. Three cases are cited in which little or no vomiting occurred this fact made it unnecessary to employ gastric lavage, the diet given in each case consisted of dextrose lemonade for a day or two, followed by diluted milky feeds, and proceeded to a semifluid diet for several weeks. The first and third patients were ultimately able to take a light diet differing little from that of other members of the household, but care was taken to avoid all foods calling for prolonged gastric digestion The principal function of the stomach is to secure liquefaction of the food, recognition of this function enables one to classify the foods requiring prolonged gastric digestion with considerable exactitude, liquefaction does not connote solution, but the chyme is a thin fluid having the consistency of weak gruel. Success can seldom be achieved unless the patient with pyloric stenosis realizes that the diet he is given has been chosen in the not altogether optimistic hope of avoiding surgical operation

Ulcer

Gastroduodenal Ulcerative Disease

—In a collective review of the literature for the years 1934 to 1936, inclusive, S J Fogelson⁸⁹ concludes that the subject of gastroduodenal ulcerative disease is characterized by a divergence of views on almost every phase of the subject. It is possible to prove or to disprove with authoritative data from qualified sources almost everything known on the subject. With the physiologists still groping, the clinicians need not apologize for their small percentage of failures

Notwithstanding the best efforts of internists, there are patients with ulcer who require surgical therapy Surgeons are today reporting better end-results with a lower surgical mortality in this type of patient. This progress has followed a specific interest in the subject on the part of surgeons who are now concerned with more than the surgical technic A qualified surgeon must be able to assay the thoroughness and effectiveness of previous medical therapy, must understand the partictular patient's gastric physiology, physic constitution, and economic status, and he must appreciate that there are times when surgery is indicated, as well as times when surgery tempts disaster When all of these factors are correlated with the local findings at operation, the surgeon should then, and only then, select that type of

surgical intervention which in the light of his own previous experiences has been most satisfactory. A continued improvement of the end-results of surgical therapy of gastroduodenal ulcerative disease may be anticipated because more surgeons are now aware of their responsibility in the guidance of all phases of therapy for the patient with ulcer

Gastric Ulcer—The changes and results of a decade in the management of gastric ulcer is given by H. L. Segal and W J M Scott 90 The review is based upon the cases of gastric ulcer admitted to the Strong Memorial and Rochester Municipal Hospitals, from January 1, 1926, to January 1, 1936 After all doubtful cases were excluded, there were 107 proved cases of gastric ulcer In these 107 cases, 66 were found at autopsy They had given no symptoms and were therefore considered incidental This leaves a total of 101 cases for clinical study

The largest number of cases occurred in the middle-aged patients, from 40 to 55 years of age. The males outnumbered the females 65 to 1. Twenty-two had perforations, 23 major hemorrhages, and 15 marked retention of a six-hour meal. In seven of the patients, the lesions were diagnosed as benign, and later proved to be malignant, 11 were diagnosed as malignant, and subsequently proved to be benign.

Thirty-seven patients were treated surgically. These do not include the 18 patients operated upon for perforation. Thirty-four of these patients had subtotal gastrectomy of the Polya-Moynihan type, with total rehef in 28, or 82 per cent, and with four deaths, or a mortality of 118 per cent. In the 23 patients operated upon by one of the authors, the operative mortality was 4.3 per cent. These figures emphasize the importance of concentrating the responsibility for

gastrectomy. The general surgeon attempting only an occasional resection of the stomach will have a high mortality. A careful preoperative and postoperative regimen will keep the operative mortality for subtotal gastric resection for ulcer to or below five per cent.

Thirteen of the 22 patients with perforation were operated upon with three deaths, a mortality of 13 3 per cent. No patient operated on within 12 hours after the onset of the perforation died. Four patients, however, entered the hospital in shock and too late for surgery. These made a total of seven deaths, and a total mortality for perforation of gastric lesions of 31.7 per cent.

Twenty-three patients had severe hemorrhage. Three of these continued to bleed and were operated upon with one death. Fifteen of the patients whose hemorrhages were controlled by medical management were not relieved of their pain, and 11 came to surgery later with one postoperative death. The other ten were completely relieved of their symptoms. It is interesting to note that hemorrhage and perforation occur in about the same frequency in malignant and benign lesions.

A table is given of all cases diagnosed as benign gastife ulcer and later proved malignant. A study of the data in this table shows there was no particular symptom or syndrome which led to a more accurate diagnosis. Even occult blood was absent in a considerable proportion of these patients. The acid values proved of no aid in diagnosis.

The general routine used in determining whether a lesion was benign or malignant was a medical trial for definite improvement, as outlined repeatedly in the literature of Jordan and Lahey. "If under a definite medical régime the niche fails to disappear, or symptoms and the niche recur or increase in size,

then that patient belongs to the surgeon without any further delay" The authors conclude, "Any uncomplicated lesion resembling gastric ulcer, no matter the size of the niche, is not a surgical case until this procedure has been tried. One can err either by rushing into surgery too soon or by continuing medical treatment too long With this régime the patient is given a fair deal Even if there are immediate reasons for instituting surgery, for economic conditions, etc. a medical régime before the operation reduces the edema and inflammation to a great extent and offers the surgeon a much better operable patient "

Another change and its result noted in this study is that although gastroenterostomy with local excision gave no mortality in the few cases in which it was done, the morbidity was high, the total relief was low, and the recurrence of malignancy, when present, was almost certain It is now agreed in this clinic that a *subtotal gastrectomy* with removal of all the glands possible is the operation of choice. The Polya-Moynihan type of gastrectomy is usually preferred. The total relief obtained from this operation was 82 per cent, and the mortality was about five per cent.

Postoperative Jejunal Ulcers—The prevention of postoperative jejunal ulcers by diet and fundusectomy is discussed by G B Fauley and A C Ivy 1 These experiments were carried out on dogs, by doing a fundusectomy (Fig 57) three or four weeks prior to the Mann-Williamson operation (gastrojejunostomy and drainage of bile and pancreatic juice into the last 15 centimeters of the ileum) The Mann-Williamson operation produces an experimental ulcer which is believed to be quite analogous etiologically to postoperative jejunal ulcer in man

The authors summarize their work by relating that fundusectomy has some prophylactic values in the prevention of jejunal ulcer in dogs operated upon by the Mann-Williamson technic and fed an ordinary diet

It was found that the feeding of an easily assimilable diet to non-fundusectomized Mann-Williamson animals delayed the onset of jejunal ulcer and of lethal perforation and hemorrhage

The combination of the special diet and fundusectomy prevented the development of jejunal ulcer in all of 13 animals, six of which survived two years or longer Gastric analyses revealed a gastric acidity of normal values in the animals surviving for more than two years, but the acid "available" for more prolonged irritation of the jejunum was definitely less in the fundusectomized than in the non-fundusectomized animals

These experimental therapeutic results emphasize the importance of the nutritional (disturbance of digestion) and particularly the acid factors in the causation of postoperative jejunal ulcer

Hemorrhage—A study of gross hemorrhage from peptic ulcer at the San Francisco Hospital has been made by L. Goldman⁹² concerning 1025 entries of 890 patients from January 1, 1928, to December 31, 1934

Incidence and Mortality — Three hundred and forty-nine patients entered the hospital because of gross hemorrhage from peptic ulcer or developed this complication during the period of hospitalization Of this number 39 (11 1 per cent) died of exsanguination, while an additional 17 (49 per cent) died of conditions associated with the bleeding, such as perforation of the ulcer, pneumonia and cerebral or cardiac thrombosis, thereby bringing the total mortality of gross hemorrhage from peptic ulcer to 15 per cent

The incidence of gross hemorrhage reaches its peak during the fifth decade, and seven tenths of the hemorrhages occur after the age of 40 years. The average age of the patients who died was 54 years, and the highest mortality was between the ages of 40 and 70 years when anteriosclerosis plays a part. There is an abrupt rise in mortality after the second hemorrhage. Approximately 40 per

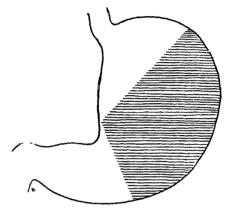


Fig 57—Shaded area shows approximately the amount of fundus removed (Drs G B Fauley and A C Ivy The Prevention of Postoperative Jejunal Ulcers by Diet and Fundusectomy, in Surgery, Gynecology and Obstetrics Dec., 1936)

cent of patients had had at least one hemorrhage before onset of illness for which they entered the hospital

Pathology—By its very nature, it must be assured that an ulcer which erodes a blood vessel and produces a gross hemorrhage is active and progressing. Ulcers in the stomach or along the anterior wall of the duodenum are more likely to heal early than those in the posterior wall of the first or second portion of the duodenum. The latter show more tendency to become chronic and to cause severe bleeding. The invasion of the retroduodenal and pancreatic tissue by an ulcer in the posterior wall of the duodenum causes an inflammatory process with adhesions to the periduo-

denal structures, thereby holding the ulcer open and enhancing chronicity. Fatal hemorrhage usually is caused by erosion of a large artery along the posterior wall of the first or second portion of the duodenum where it overlies the pancreas Bleeding from a gastric ulcer usually arises from one of the coronary vessels of the lesser curvature because the vessels he between the layers of the lesser omentum closely applied to the wall of the stomach Severe bleeding from ulcers of the greater curvature is rare because of the infrequency of benign ulcers at this site and the fact that the gastroepiploic artery is not in direct contact with the wall of the stomach

Treatment—The immediate treatment of gross hemorrhage from peptic ulcer is essentially a problem both for the internist and for the surgeon, requiring close co-operation between them. By an understanding of the basic principles of therapy, hemorrhage might be controlled in a greater number of cases. Opinion is divided about many aspects of the management of such patients, but experience in the University of California Surgical Service at the San Francisco Hospital has led them to conform, in general, to the following plan.

- 1 The patient should be kept absolutely quiet in bed and, it shock is present, should be treated accordingly as complete immobility as is possible should be maintained.
- 2 Morphine should be given in large enough doses to bring about mental and physical rest as well as to allay gastric peristalsis. It may be used in conjunction with atropine for the first few doses in an attempt to relax the muscularis and inhibit the formation of gastric secretions.
- 3 Frequent determinations of the blood pressure, hemoglobin and red

blood cell count should be made during the critical stages

- 4 Food by mouth should be withheld. As long as the patient is ingesting material into his stomach, gastic peristalsis is stimulated and, with the stimulation of peristalsis, permanent clot formation is attained with difficulty. The taking of food likewise stimulates the secretion of gastric juice, which is unde-Alkaline powders, however. may be administered Feeding should be resumed only when there is conclusive evidence that the hemorrhage has stopped and has not recurred for at least 48 hours, as evidenced by the increasing blood pressure, the lowered pulse rate, rise in hemoglobin, and the general appearance of the patient. If the hemorthage has ceased, small feedings may be instituted and gradually increased to a full Sippy regimen
- 5 During the first 24 to 48 hours, parenteral fluids should be withheld in order not to decrease the viscosity of the blood. No fluids are given intravenously, except blood, during the active bleeding phase, as the rise in blood pressure may stimulate further bleeding. After the first day or two, saline solution, with or without dextrose, may be given by subcutaneous infusion or rectal drip.
- 6 There are many contradictory opinions concerning the values and dangers of the transfusion of blood, and some feel that it is better not to transfuse for fear of raising the blood pressure and causing further bleeding. Though, in this series, only five per cent of the patients who died from bleeding peptic ulcer had received transfusions of blood, this procedure is recommended for the reasons to be set forth. In the patients who died, the average length of life after the onset of bleeding was four and one-half days. In other clinics where trans-

fusions have been used more freely, the average length of life was 16 days These comparative figures suggest that many hemorrhages can be controlled by transfusion. Allen and Benedict reported that in their opinion the transfusion of blood aided in checking the hemorrhage far more often than it started bleeding again, they advocated the transfusion of 300 cc of citrated blood when systolic blood pressure dropped below 70 mm of mercury Hurst and Stewart agreed that all patients should have the benefit of transfusions when the hemoglobin dropped below 40 per cent In deciding whether or not a patient requires transfusion after an initial hemorrhage, Lahey estimated whether that patient could withstand another such hemorrhage If it seems that a second hemorrhage probably would be fatal, the blood stream is replenished at once

In Goldman's opinion, therefore, when a patient continues to bleed after adequate medical treatment, the slow administration of from 200 to 300 cc of blood should be instituted before his blood pressure, hemoglobin and red blood cell count reach a hazardously low level The beneficial effect on the anoxemia as well as on the mechanism of coagulation outweighs the possible dangers of transfusion Obviously a suitable donor should be available at all times, as the patient may suddenly bleed considerably The use of while under observation transfusions during the later stages encourages more rapid convalescence

7 The administration of so-called coagulants, such as thromboplastic substances or calcium, has no effect on the hemorrhage. The administration of epinephrine or astringents by way of a stomach tube probably has no effect if the bleeding is very severe.

8. Gastric lavage during bleeding from peptic ulcer has been advocated by some,

but it is felt that this should be reserved for those patients in whom the stomach becomes distended by the accumulation of blood clots. The tendency of lavage to break up a fresh clot and provoke further bleeding is too great to justify the use of this measure in a routine way.

If the foregoing regimen fails to stop the hemorrhage and bleeding persists or recurs while the patient is still fasting, it is believed that early surgical intervention is indicated

Prognosis—The prognosis for recovery on conservative treatment is poor in patients who continue to have serious hemorrhage or in whom repeated hemorrhages occur in spite of proper medical treatment (including the transfusion of blood) This is especially true in the patient over 40 years of age. One would like to defer surgery, if possible, in such cases, but it is probable that some form of surgical intervention will be necessary if the patient's life is to be saved

Judgment of each case on its own merits is essential. The patient in question may have only a 20 to 30 per cent chance of surviving under further conservative treatment. One can reasonably assume that he is bleeding from a large artery, and the longer one waits the less his chance of survival will be Three patients in the series were operated on too late during the acute bleeding phase -ten days or longer after the onsetwith 100 per cent mortality. After from one to two weeks of intermittent or continuous bleeding, transfusions afford very temporary benefit and the patient is poorly nourished, has a poor coagulating mechanism and is a poor surgical risk For all these reasons, earlier surgical treatment in this type of case is urged

Surgical Consideration—If operation is done during the phase of acute bleeding, a direct attack on the ulcer is

advisable in most cases. If the ulcer is in the stomach, the vessels on all sides should be ligated and the ulcer sutured; or, if the patient's condition permits, it should be excised and gastroenterostomy performed In the treatment of duodenal ulcer, excision may be impossible, since many of these ulcers are on the posterior wall of the duodenum Because of the higher incidence there, ulcer of the duodenum should be suspected if the stomach appears to be normal The operation devised by Allen and Benedict is the procedure of choice when surgery is indicated for bleeding duodenal ulcer during the acute phase. The stomach is transected between clamps at the prepyloric region, and the duodenal end is elevated The blood vessels entering the ulcer are ligated outside the duodenal wall and the duodenal end is turned in An anastomosis is then performed between the stomach and the jejunum. This affords the greatest protection against recurrence of the ulcer or subsequent hemorrhage Suturing the bed of the ulcer in the posterior wall of the duodenum is not practical because of the triability and fixation of the inflamed tissue. It is at such a time that one's surgical judgment must be the deciding tactor Castroenterostomics have been done during the acute phase, with cessation of hemorrhage, when attacking the ulcer directly did not seem feasible. In a high percentage of cases in which this method is used, however, recurrence of the hemorrhage takes place

It is felt that in the case of a first hemorrhage, the patient should be given a chance for relief under medical care unless he was following a strict regimen at the time the bleeding began. If hemorrhage recurs, however, surgery is indicated during a quiescent state. Even though transitory healing has taken place and roentgen examination after from

three to four weeks of medical care fails to demonstrate the presence of an ulcer, the lesion may recur at the same site At operation during such a stage, only a small dimple may be seen at the site of the previous erosion.

When the operation for bleeding peptic ulcer is done in the quiescent stage rather than during a phase of active bleeding, the procedure of choice, if the patient's condition and other factors permit it. is removal of the area around the ulcer by partial gastric resection with anastomosis of the proximal portion of the stomach to the jejunum This procedure removes the vulnerable portion of the duodenum and brings about such profound changes in the gastric physiology that the mechanical and chemical factors which were chiefly responsible for ulceration are more or less completely and permanently controlled, thereby offering freedom from recurrence in the majority of cases Indirect procedures such as gastroenterostomy or pyloroplasty, are followed by a relatively high percentage of recurrences as well as by the added danger of gastrojejunal ulcer, but the operative mortality is relatively low The direct procedure of partial gastric resection, on the other hand, carries a higher mortality but a lower incidence of recurrence Many times induration and inflammatory reaction about the duodenum cause difficulty in its inversion In such cases it is probably advisable to allow the ulcer to remain and to transect the duodenum proximally, ligate the vessels and perform a gastric resection Surgical judgment of all the factors involved must determine the procedure to be undertaken

Perforation — According to D A Lemberg, 93 there were 233 cases of perforation of gastroduodenal ulcer in which operation was performed at the Emergency Institute of Leningrad from 1932

to 1935 There were 22 men and 11 women In 29 cases (124 per cent) there was no history of ulcer symptoms in the past or prior to the attack. Thirty-three (286 per cent) manifested exacerbation of the symptoms in the days preceding the perforation Sudden onset of severe epigastric pain, absence of abdominal breathing, rigidity of the abdominal wall and pneumoperitoneum constituted the most reliable diagnostic signs

Treatment-This consisted of a simple suture of the perforation in two layers, the omentum being utilized to protect the suture line, and closure of the abdomen without drainage When the perforation was located in the pylorus or in the duodenum, a gastroenterostomy was added The mortality was 167 per cent The author is opposed to partial gastric resection on the ground that wide application of it would result in high mortality. He is not convinced that resection is the best form of treatment for every type of ulcer The author believes that the fact that Yudin was able to show the low mortality of 98 per cent in 673 resections is due to selection of cases, otherwise it would be difficult to explain the same author's 534 per cent mortality from simple suture He concludes that the palliative procedure of simple closure with or without gastroenterostomy is capable of saving many lives and of curing a fairly high proportion of cases Patients with late ulcer symptoms following palliative procedure may be subjected to a medical regimen or to a resection under much more favorable conditions

Perforation of Gastrojejunal Ulcer—The article by C G Toland and H L Thompson⁹⁴ consists of a detailed review of the literature and a report of ten new cases The term "gastrojejunal ulcer" is used in this article to include all secondary ulcers situated at or ad-

jacent to anastomoses between the stomach and the jejunum irrespective of their gastric, marginal, or jejunal location. The qualifying term "acute perforation" is restricted in this presentation to the use originally made of it in this country and means perforation of a peptic ulcer into the free peritoneal cavity

Treatment—The active treatment of acute perforation of gastrojejunal ulcer is surgical. In neglected cases with diffuse peritonitis injudicious surgery may not only be harmful, but fatal There are two schools of thought on the cor-The adherents rect type of treatment of one school maintain that simple suture is safest and therefore sufficient for the primary operation. It may be followed by medical treatment and by radical surgery later, if necessary The members of the second school believe that in selected cases different measures are indicated If the duodenal ulcer is healed and the pylorus patent, the gastroenterostomy may be taken down and normal continuity restored. If an active peptic ulcer is present, pyloroplasty or gastroduodenostomy in the first or second portion of the duodenum. or a Polya or Billroth type of gastrectomy should be done

There were 117 cases of acute perforation included in this study, but the outcome was not recorded in three. In the remaining 114 cases, 34 deaths occurred, a mortality of 29.8 per cent.

From the results obtained, the authors conclude that surgery and not expectant treatment, is indicated in acute perforation of a qustrojejunal ulcer. Disconnection of the gastrojejunostomy appears to be the safest procedure and should be carried out when the patency of the pylorus permits. Simple suture resulted in a mortality of 17.6 per cent, and required more secondary operations than the other procedures. Its simplicity, how-

ever, makes it applicable to the largest number of cases. Gastrojejunostomy resulted in a mortality of 285 per cent, and in view of the findings, it was not only ineffectual but also meddlesome. It is contraindicated except when pyloric obstruction is present. The authors believe that the most remarkable finding with respect to treatment of acute perforation of gastrojejunal ulcer was the fact that in 17 cases wherein pyloric resection was carried out there was only one death, representing a mortality of 56 per cent.

Subacute Perforation—Subacute or minor perforation is a much milder affair than the acute Usually the actual perioration is preceded by a period of increased ulcer activity, often the perforation itself is considered to be merely a manifestation of the increase of activity A M Dickinson95 states there may be pain and tenderness in the cpigastrium, there is absence of the severe pain and shock seen with acute perforation. There may be vomiting but this is usually of short duration and often by the time the physician sees the patient, he finds the latter taking fluids by mouth with no apparent discomfort. Within a few hours after the onset, the patient appears quite comfortable and exactly what has occurred may be a matter of speculation. A great percentage of these minor perforations go on to spontancous recovery and the patient is apparently completely well in three to four days. That there has been a subacute perforation may be proved by the finding of free gas in the peritoneal cavity by fluoroscopic examination in the early stages, later the diagnosis may be established by operation or radiography The mildness of the symptoms following minor perforations may be explained upon the basis of a small amount of leakage and the ability of the peritoneal

surfaces to cope with such foreign material. It is true that many of the minor perforations are promptly plugged by mucus or sealed by omentum; this does not occur in all instances, however; occasionally subsequent radiography or operation demonstrates that the perforation is still patent. The size and position of the ulcer apparently have little to do with the severity of the symptoms resulting from perforation

Subacute perforations of peptic ulcers are very commonly mistaken for other conditions. The symptoms are quite frequently thought to be due to gastritis, pleurisy, central pneumonia, coronary heart disease, gall bladder disease, etc.

From the literature on peptic ulcer one gathers the impression that subacute perforations are relatively infrequent. The fact is, that they are frequent enough but we fail to recognize them. In their study of this problem, Singer and Vaughan found that 14 cases of subacute perforation in comparison to 12 cases of acute perforation, were admitted during a three months period at Cook County Hospital. This would seem to indicate that the frequency of these two types of perforation is about equal.

Treatment of the acute perforation of a peptic ulcer is based upon immediate operation at which time the ulcer is excised or destroyed by cautery, the ulcer bearing area inverted and the suture line covered with a tab of omentum, in some hands, a gastroenterostomy is also done at the same time. Most surgeons feel that acute perforations are surgical emergencies and that unless operated upon promptly, patients soon become moribund. Without operation at least 85 per cent of these patients will die

What then is to be the method of treatment of the subacute perforation. To be logical, the same method is indicated. On the other hand, it is an estab-

lished fact that a very considerable percentage of the patients with subacute perforations do recover without the bene-Singer and Vaughan fit of surgery reported a series of 40 such cases which occurred in a period of 18 months at the Cook County Hospital However, there are some instances in which surgery is positively indicated if the patient is to recover Where the perforation closes spontaneously and there is mild peritoneal reaction, probably the patient will recover without surgery The crux of the dilemma is to decide if the perforation is closed or not. This may be almost impossible. A safe rule is to operate upon all cases within the first 24 hours, where a diagnosis of perforation is established If more than 24 hours has elapsed since perforation occurred and the process is apparently quiescent, operation should be deferred for it will only stir up infection and lead possibly to a fatal peritonitis on the other hand, there is evidence of spreading peritoneal irritation operation is indicated even though more than 24 hours has elapsed since perforation

Results in Acute Perforated Peptic Ulcer Treated by Simple Closure—The results in 74 cases of acute perforated peptic ulcer treated by simple closure are reported by M. A. Sallick 66. The patients were admitted to the Beekman Street Hospital, New York, between 1926 and 1933, inclusive. A postoperative period of at least 12 months had elapsed in each case considered Thirty-four of the patients were examined recently and of the remaining 32. 13 answered a questionnaire. A total of 45 patients were therefore available for study.

It is interesting to note that all of the 74 patients were males, that 41 of the ulcers were prepyloric, 26 duodenal, and seven pyloric Eighty-six per cent of all

the patients had a previous ulcer history and 63 of the 74 presented a clinical picture so typical that the diagnosis could readily be established. Of 11 patients remaining, three presented difficult diagnostic problems. Two were believed to have coronary disease, one an intestinal neoplasm with pyloric obstruction.

The 74 operations were performed by nine surgeons. They made a simple closure, usually with a purse-string suture, but in some cases they used a mattress or figure-eight suture. As a rule there were three suture layers and the omental tab was included in the last one. The total mortality was 10.8 per cent.

The results were classified as good, bad, and fair. In the cases with good results the patients remained symptomfree after a reasonable period of dietetic In the cases with and hygienic care poor results the patients reported periodic recurrences regardless of whether the symptoms were true ulcer symptoms or severe In the cases with fair results the patients reported recurrence of the symptoms, but they were mild, inconstant, and not entirely typical of ulcer By these standards 15 of the 32 patients who were followed-up and examined, presented poor results, six fair, and nine good. The symptoms recurred in 23 of the 32 patients (717 per cent) questionnaire report on the 13 patients showed five poor, one fair, and seven good results. Six of these patients (46 per cent) had recurrence of the symptoms. In the total group of 45 patients, 29 (64 per cent) presented further significant gastric symptoms. In addition, five of these 45 patients required some additional surgery

From the data presented the conclusion is drawn that routine use of simple closure, with its low mortality rate and excellent early results, is justified in the emergency treatment of acute peptic ul-

cer perforation Gastroenterostomy is rarely indicated because of mechanical reasons, no matter how extensive the induration nor how great the apparent pyloric distortion after plication. Acute perforation followed by successful closure affords a permanent cure of the ulcer in only a minority of the patients

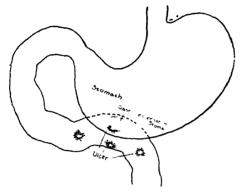


Fig 58—The common locations of gastrotejunal and jejunal ulcers following gastroenterostomy (Courtesy J A M A, Oct 23, 1937)

because in almost two of every three cases peptic ulcer will recur later with greater or lesser severity

R Lewisohn⁹⁷ points out that many patients have persistent ulcer symptoms after suture of an acute perforation These symptoms are due to the fact that the anterior wall ulcer persists in spite of the previous perforation or that in addition to the anterior ulcer which perforated acutely and was sewn over, a posterior wall ulcer existed which, of course, was not affected by the surgical procedure. The diagnosis must be made on clinical grounds, as the roentgen-ray examination will show distorted duodenal bulbs in all cases in which patients were subjected to a previous operation on the duodenum If severe ulcer symptoms persist after the suture of a perforation has been done, patients should be reoperated upon and a partial gastrectomy should be carried out.

Partial Gastrectomy for Gastric or Duodenal Ulcer-Subtotal gastrectomy has become a well recognized and established procedure in the surgical management of gastric and duodenal That it has become a controversial subject cannot be denied According to S F Marshall and E D Kiefer,98 there are, on one hand, surgeons who are highly enthusiastic for the more radical methods and, on the other, those who advocate more palliative operative procedures The authors believe that somewhere between these two points of view, at least today, rests a satisfactory position but that partial or subtotal gastrectomy is the method of choice when limited to properly selected cases It naturally follows and should be emphasized that it is impossible for one method to fit every patient or every type of ulcer

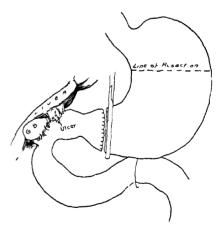


Fig 59—A densely adherent duodenal ulcer left in situ because of technical difficulties. The stomach was divided in the prepyloric area and a high subtotal gastrectomy performed (Courtesy, J. A. M. A., Oct. 23, 1937)

Two hundred and forty-two patients were operated on for gastric, duodenal or gastrojejunal ulcer in the Lahey Clinic in the ten years from January 1, 1927, to December 31, 1936 This number does not include patients with

acute perforation The type of ulcer and the method of treatment for the 242 patients is shown in the accompanying table

Indications—Certain clinical features have proved to be definite indications for surgical intervention in the management of patients with duodenal ulcer. It is obvious that acute perforation requires immediate surgical intervention, and this fact needs no comment. Patients with intractable ulcer, who for one reason or another fail to obtain relief with adequate medical care, are forced to sub-

cessful medical management Recurrence of gross hemorrhage in spite of adherence to a regimen for ulcer is a definite indication for surgical intervention, since the prognosis with continued medical management is poor. Since gross hemorrhage is a serious complication in patients with ulcer, carrying with it a definite mortality rate of at least five per cent, we have established the policy of advising surgical treatment for patients with serious recurrent hemorrhage

The indications for surgical intervention in cases of gastric ulcer are some-

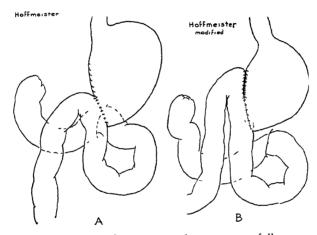


Fig 60—A, the Hoffmeister type of gastrojejunal anastomosis following subtotal gastrectomy B, a modification of the Hoffmeister anastomosis reinforcing the closed end of the stomach with jejunum. This is considered the procedure of choice (Courtes), J. A. M. A., Oct. 23, 1937.)

mit to operation for control of their Pyloric obstruction occurring with symptoms of active ulcer is commonly due to spasm, infection or edema, and in most instances can be relieved by rest, diet, and alkalization ever, recurring bouts of acute ulcer produce narrowing of the pylorus, shortening of the duodenum by scar formation and real cicatricial stenosis, which necessitates surgery From a statistical study by one of the authors of a large series of cases of duodenal ulcer, gross hemoirhage was found to indicate a somewhat more severe type of ulcer and its presence to decrease the probability of sucwhat different because of the different clinical features of gastric lesions in contrast to duodenal ulcer and particularly because of the diagnostic difficulty in distinguishing between some gastric ulcers and early carcinoma. It has been definitely established and reported by Dr Sara M Jordan of Lahey Clinic that a large percentage of gastric ulcers will heal readily and completely with medical treatment. Surgical treatment is therefore indicated only for the gastric ulcer which because of the large size of the crater or extension into adjacent tissue proves intractable with medical measures and for the ulcer which be-

cause of insufficient tendency to heal during medical management is suspected of being an early carcinoma. Obstruction is rarely an indication for operation in cases of benign lesions. Dr. Jordan has repeatedly shown that the most practical method of differentiation between benign and malignant gastric lesions is to employ a period of medical treatment for ulcer with repeated x-ray examinations of the stomach.

The greatest benefit accomplished by the surgical management of ulcers results from the change in the gastric secretory and motor function, and there is little doubt that, of all operative procedures, partial gastrectomy best accomplishes this change. The decrease of the gastric acidity with this operation is due. (1) to rapid emptying, with a decrease of the gastric secretory phase; (2) to a reduction of the secretory mucosa, and

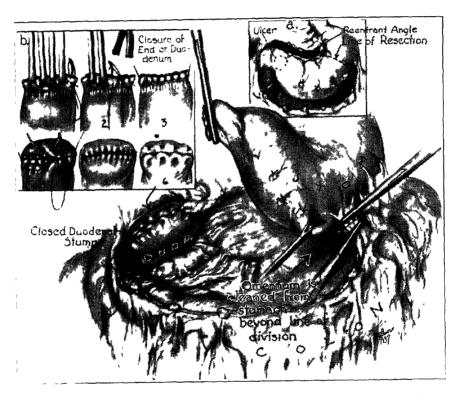


Fig. 61—The storach is mobilized and the duodenum divided, a, line of resection of the stomach, b method or closure or the duodenal stump. (Courtesy, J. A. M. A., Oct. 23, 1937.)

The preoperative decision pertaining to the nature of a gastric lesion is often of more value than the decision made at time of surgical exploration. As has been frequently declared by Dr. Lahey, it is often impossible at the operating table to tell whether the lesion is benign or malignant. Consequently, a radical removal must be done unless preoperative data have determined the nature of the ulcer.

(3) to neutralization of gastric acidity by the regurgitated alkaline duodenal contents

Partial gastrectomy is an operation of considerable magnitude beset with many technical difficulties and may be accompanied by a considerable mortality even in the hands of the most experienced and skilful surgeons. In the authors' earlier cases the mortality of this operation ran prohibitively high, with a rate

of 18 per cent, but with an increasing experience in the technical details and with a better selection of cases the mortality should certainly not be much greater than that associated with gastroenterostomy. During the past year there have been four deaths in 34 cases, which is a mortality of 11 per cent. This rate is undeniably high, but it is frequently unfair to compare the mortality rates of two series of cases on a strictly percent-

the duodenum or near the pylorus present few technical difficulties and are comparatively easy to remove, and with them the mortality should not be higher than that associated with gastroenterostomy

The technical difficulties of such a formidable operation as partial gastrectomy are considerable and are to be surmounted only by an extensive experience with gastric surgery. Once having

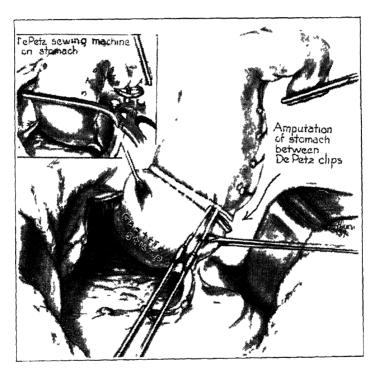


Fig. 62—The stomach is divided by cautery between the double row of clips applied by the $\frac{1}{16}$ Petz clamp. Insert shows the application of the de Petz sewing clamp. (Courtesy, J. A. M. A., Oct. 23, 1937.)

age basis. Two prominent groups of factors influence the death rate for subtotal gastrectomy, first, the technical factors relating to the operation and the anesthesia and, second, the group of factors pertaining to the general physical condition of the patient and to the pathologic picture of the ulcer, including its size, depth, location and chronicity and the involvement of surrounding tissues. Ulcers situated on the anterior wall of

decided on a radical attack on the ulcer, one should really carry out a radical removal of the stomach. While pylorectomies and antrumecties have a mortality rate as high as partial resection, they have little advantage over a gastroenter-ostomy, because they fail to remove a sufficient amount of the stomach and consequently fail to decrease gastric acidity. Partial gastrectomy involves removal of at least three-fourths or four-

fifths of the stomach The operation should be radical enough to produce anacidity, and a recurrence of symptoms may follow the failure to obtain this result

Provided resection of the stomach has been sufficiently radical, it is believed that it makes little difference what type of anastomosis is made. The Billroth I type of procedure frequently cannot be

Complications—The most disturbing complications were those of a pulmonary character such as pneumonia, pulmonary edema and atelectasis, which accounted for 50 per cent of all fatalities. Hemorrhage rarely occurred. Failure to control all bleeding points at the time of operation is responsible for most cases, although sloughing of the suture line may occasionally cause hemorrhage, and twice

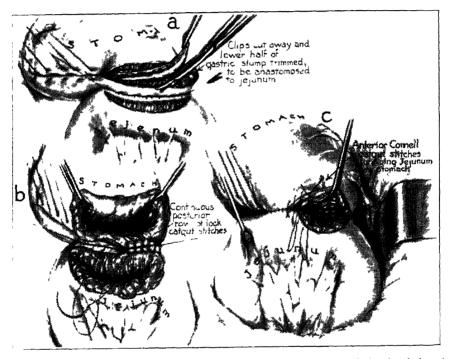


Fig. 63—Hoffmeister method of gastrojejunostomy, the upper half of the divided end of the stomach is closed inverting the clips. The jejunum is sutured to the remaining portion of the stomach. The clips are cut away in this are i and the jejunum is incised, forming the stoma, the inistomosis is then completed. (Courtesy J. A. M. A., Oct. 23, 1937.)

used with the large adherent, croding ulcers, which do not permit sufficient mobilization of the duodenum to make possible anastomosis of the duodenum without tension to a radically resected stomach. Many modifications of the Billroth II method can be utilized safely and satisfactorily. The authors have gradually come to employ a modification of the technic as proposed by Hoffmeister and have found it most satisfactory.

the authors have seen fatalities result from this. They admit from their experience that the so-called hemostatic stitch put in the cut stomach wall does not protect all patients from postoperative bleeding, and they have for some time practiced ligation of all vessels in the divided end of the stomach

Intra-abdominal infection accounts for a small percentage of deaths, but it is believed that if soiling from spilled gastric contents were eliminated, peritonitis would be an infrequent cause of postoperative mortality. One death was due to perforation of the stoma due to the giving way of the suture line, but with the employment of silk suture material in the outer layers, this should not occur.

Intestinal obstruction following partial gastrectomy is usually caused by edema in the mesocolon and most commonly occurs in the distal loop beyond the point of anastomosis. When gastric stasis persists beyond eight or nine days, edema is usually not the cause and the failure to drain is usually due to obstruction in the jejunum, reoperation then must frequently be carried out

Results—The final clinical results are quite satisfactory and compare favorably with the end results of any major surgical procedure. Of the series of 102 patients on whom gastric resection was done, 74 were accurately followed, and the results in 84 per cent can be classified as good or excellent. The patients are well, almost as robust as ever and live under few dietary restrictions. In ninc per cent the results were recorded as fair or poor. These patients have symptoms which are apparently caused largely by functional disorders of the gastrointestinal tract or by neurasthema.

Five patients, or 67 per cent, had postoperative ulcer, three have recovered with surgical help and are now well. One is still an invalid, and the fifth has not returned to the clinic although it is reported that he has had three hemorrhages. It is the general experience that postoperative ulcer is associated with persistently high gastric acidity.

It is important to strive for postoperative anacidity because of the occurrence of jejunal ulcer in patients in whom the acid has not been sufficiently reduced by partial resection. Unless anacidity or hypoacidity is produced by high resec-

tion, it is difficult to see any clinical advantage of this operation over gastro-enterostomy.

Tumors

Benign Tumors of the Stomach— J F. Minnes and C F. Geschickter⁹⁹ report the clinical and pathological features of 50 benign tumors of the stomach recorded at the Johns Hopkins Hospital, Baltimore, in the period from 1889 to date

Benign tumors may arise from the mucosa, submucosa, muscularis, or serosa of the stomach According to the tissue of origin they may be divided into two groups: the epithelial and the Among the epithelial mesenchymal tumors are adenomas, adenopapillomas, adenomyomas, and fibro-adenomyomas Chief among the mesenchymal tumors are the leiomyomas, fibromas, lipomas, neurofibromas, and the rare angiomas and ostcomas Finally, there is a group of lesions, which, though usually included with tumors, are not truly neoplastic These include simple blood or lymph cysts, dermoidcysts, echinococcus cysts, and embryonic rests of pancreas

Of the benign tumors of mesenchymal origin, the leiomyomas are by far the most common Neurofibiomas are not Hemangiomas are much infrequent Cysts other than simple cysts are extremely rare. Of the 26 cases of polypoid tumors reviewed by the authors, the neoplasms were multiple in more than 50 per cent While benign tumors do not occur much more frequently in one part of the stomach than another, they are slightly more common in the pyloric region than elsewhere. In the reviewed cases the majority of the neoplasms were the size of a pea or smaller Only two were as large as a hen's egg One of these was a neurofibroma situated at the cardia and the other an

adenoma located in the pyloric region. The mesenchymal tumors may be sessile or pedunculated. They lie within the wall of the stomach, project into its lumen, or remain subserous and project into the peritoneal cavity. They are usually small, but sometimes grow to a tremendous size.

The epithelial tumors may be divided into two groups—the adenomas and the adenopapillomas—The adenomas arise from the mucosa as reddish friable, button-like or lobulated masses. The adenopapillomas form cauliflower-like projections of varying size within the lumen of the stomach. They are friable and frequently ulcerated. It is tumors of this type that may cause pyloric obstruction. There is considerable evidence in the literature to show that being adenomas and adenopapillomas may develop into cancer.

Of the benign tumors reviewed by the authors 26 occurred in white and 23 in colored patients. The ratio of males to temales was 39.11. The voungest patient was 21 years of age and the oldest 14. The tumors developed most frequently in the fifth and sixth decades of life. Their maximum incidence was between the 75th and 80th years.

In the diagnosis little reliance can be placed upon the clinical features Symptoms, when present, are dependent upon a complication such as obstruction, ulceration or hemorrhage. The size and position of the tumor are important. The tumor is rarchy large enough to be palpable through the anterior abdominal wall Not infrequently, tenderness and muscle spasms in the epigastrium are noted. The hydrochloric acid content of the gastric juice is of equivocal value As a rule it is diminished or entirely absent, but there are reports of cases in which it was increased. The frequency of correct diagnosis of benign gastric tumor has been increased by expert roentgen examination of the stomach

As the sudden development of a complication, such as hemorrhage, may cause death, as annoying and even dangerous symptoms or complications may occur at any time, and as tumors of the epithelial group not infrequently become malignant, benign neoplasms of the stomach should be removed as soon as they are recognized If the tumor is single and circumscribed, simple excision with a good margin of healthy tissue will suffice, but in cases with multiple tumors scattered diffusely over the gastric mucosa, resection of the stomach sufficient to remove all of the diseased area should be done

The article of R Kaijser¹⁰⁰ gives an excellent résumé of the observations and reports on hemangioma of the gastro-intestinal canal in the medical literature. In addition to about 60 cases of this nature in the literature, the author adds two from his own personal material

The first case was that of a girl 19 years of ago who appeared to have been badly afflicted with hereditary tuberculosis and disclosed, in addition to a number of congenital hemangiomas of the skin and buccal mucosa, a large cavernous hemangioma of the stomach near the lesser curvature. Radical attack on the gastric mass could not be attempted because of its extent and therefore it was treated by roentgen irradiation. The bleeding into the gastrointestinal tract became less and the severe anemia improved.

In the second case there was a cavernous hemangioma showing a roentgen shadow defect in the sigmoid colon of a boy eight years of age. In this case the affected section of the intestine could be removed. The bleeding into the intestine stopped and a cure followed.

In both cases, in addition to the bleeding into the intestinal tract, there was a deposition of calcium in the cavernous spaces, phleboliths, which was roentgenologically demonstrable. These phleboliths are often found in the small pelvis, but practically never in the other regions of the abdominal cavity.

The treatment of such growths is purely surgical. When, as is frequently the case, surgical removal is impossible because the tumor does not present clearcut edges and the vascular dilatations extend widely, the outlook for the patient is quite grave, as a rule

Kaijser divides the hemangiomas reported in the literature into

- 1 Multiple phlebectasias. These are not infrequent and are always to be regarded as of congenital origin, as well as the tumors which are in the following groups
- 2 Cavernous hemangioma occurring in two different forms. The one form is found in the wall of the intestine, in which cases the intestine is invaded by the growth to a certain extent and the walls are partly replaced by tumor tissue In these cases well-marked delineation of the borders of the mass is absent In the other form there is a sharply delimited, frequently polypoid, tumor The latter form is often found in the colon. All these growths with their widely dilated venous loops frequently contain phleboliths and may often be recognized roentgenologically by the latter
- 3 Simple hemangioma or capillary hemangioma These consist of a network of more or less dilated capillaries and in addition, of cells originating from the endothelium of the capillaries. They may become cell-rich tumors and form the transition to the hemangio-endotheliomas. They may grow to become large

tumors, obtruding into the stomach and the lumen of the small or large intestine.

4 Angiomatosis. This condition appears under different forms, one of which is the Rendu-Osler disease, telangiectasia hemorrhagica hereditaria. The condition shows the most variable characteristics; hyperplasia and exuberant development of the endothelium of the involved vessels play a definite rôle. Frequently the microscopic picture of the tumor suggests malignancy such as a true angiosarcoma, but it is always benign. As a rule this type of tumor of the intestine is accompanied by hemangiomas and warty growths of this character appear in crops Often they are tiny bluish-red nodules without pathological significance

Sarcoma—Although sarcomata of the stomach comprise only about one per cent of all gastric neoplasms, a surprising number of cases is reported in the literature. In studying these reports, one is impressed with the difficulties which attended the clinical and roentgenological diagnosis of this condition and also with the fact that an early diagnosis is even more important in sarcoma than in carcinoma, at least from the standpoints of operability and curability

Undoubtedly, the fact that sarcomata seldom involve the gastric mucosa early and therefore produce no characteristic deformity of the stomach on roentgen examination has led in many instances to the erroneous conclusion that no neoplasm was present, in spite of the clinical evidence. In such cases the possibility of sarcoma and its different pathological process from that found in carcinoma should be considered.

Clinical Features—E N Collins and M G Carmody¹⁰¹ point out that the exogastric variety of sarcoma, which usually produce a palpable mass, may be mistaken for retroperitoneal tumor, pan-

creatic or mesenteric cyst, and because splenomegaly is present in ten per cent of cases of sarcoma of the stomach, Banti's disease also may be confused with this condition. In some of the reported cases of other varieties, the symptomatology was that of a benigh peptic ulcer. Usually, soon or late the

prone to involve the orifices of the stomach

The duration of symptoms may be longer than is the case in *carcinoma* In a series of 54 cases reported by Balfour and McCann, the average duration of symptoms was more than a year, there was evidence of bleeding in 16



Fig. 64—Case 1. Roentgenogram showing evidence of an ulcerating neoplasm. When the stomach was completely filled with barium suspension, no evidence of abnormality was apparent (Courtes). Am. Jour. of Digest. Dis. and Nutrition. Leb., 1937.)

symptoms and signs of all sarcomata of the stomach are similar to those of carcinoma. In addition to epigastric distress, the patient generally complains of weakness and loss of weight. Secondary anemia and achlorhydria are common findings, as were present in three of the authors' cases. Obstructive symptoms are rarely present because sarcoma is not

and of a palpable tumor in over half the cases In the authors' patients, the average duration of symptoms was seven months, the shortest being three weeks and the longest one year

Diagnosis — Strauss and Haggard have emphasized that the presence of hematemesis with melena in a young person and a palpable epigastric tumor

without obstruction are suggestive of the presence of sarcoma of the stomach A clinical diagnosis is seldom made preoperatively. However, we believe this lesion should be suspected in any patient, regardless of age, who has had continuous gastric symptoms and signs suggesting a neoplasm for a few months, a year or more, when the roentgenologist finds either no evidence of mucosal involvement or evidence of a large shal-

Treatment—The operability of sar-comata of the stomach is greater than that of carcinomata. When the diagnosis is established, resection of the growth is the procedure of choice. Of the 54 cases in Balfour and McCann's series, 38 were operable. At the time of their report, death had occurred in 26. The average duration of life in those who died was 11 months and in those still living, it was five years

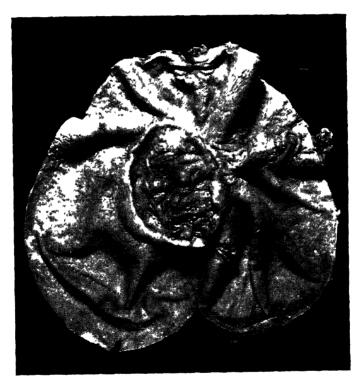


Fig 65—Case 1 Photograph of gross specimen showing a large indurated ulcer (Courtes) Am Jour Digest Dis and Nutrition Feb 1937.)

low ulceration which is not characteristic of either benign peptic ulcer or ulcerating carcinoma, especially if associated with an extralumenal mass. A saircomatous mass which involves the lumen of the stomach obviously cannot be differentiated roentgenologically from other types of neoplasm. Renshaw has recently reported a case of lymphoblastoma of the stomach with especial reference to the gastroscopic appearance.

It resection is not possible, palliative surgical measures may be employed Pack and McNeer state that all sarcomata of the stomach, except the spindle cell variety, are radiosensitive tumors. If the lesion is a lymphosarcoma, radiation therapy is especially indicated

Pattison has reported a case of diffuse lymphosarcomatous infiltration of the stomach on which a biopsy was made, and in which identification was the

sole method of treatment The patient was a boy of 20 years to whom repeated courses of *deep roentgenotherapy* were given. At the time of the report, 15 months after the operation, the patient was in perfect health and had gained 20 pounds.

When there is roentgen evidence of neoplastic involvement of the cardiac end of the stomach and operation is not performed, the possibility of using a course of roentgenotherapy as a diagnostic procedure should be considered. If "progress" roentgen examinations show definite improvement, further roentgenotherapy would be indicated, conceivably on the basis of a radiosensitive sarcoma.

Prognosis—The prognosis in sarcoma of the stomach, of course varies with the character and duration of the lesion, the presence or absence of metastases, and whether or not it is operable or radiosensitive. It is unusual for these patients to survive for more than three to five years, because metastases are often present at the time of operation or initial toentgenotherapy Earlier diagnosis may be made in the future According to D'Aunoy and Zoeller, most authorities agree that the pedunculated growths, which usually are the spindle cell type, offer a better prognosis as compared with the infiltrating varieties which are most frequently lymphosarcoma or round cell in type. The reasons which they give are that those of the spindle cell type grow more slowly, have a tendency to remain circumscribed, do not metastasize so early, and are removable. However, in a review of the literature the authors have found that patients with lymphosarcoma comprise the greatest number of those surviving over a fiveyear period

Carcinoma—According to F H Lahey¹⁰² hardly a situation exists today which challenges the pride of surgery

more than that of carcinoma of the stomach The low percentage of operability when the diagnosis is finally made and the patient is sent for operation, the low percentage of cures, and the high mortality rates of operations for its relief are all too convincing evidences that progress in this field is slow and that there is an opportunity for improvement

In a paper from this clinic dealing with 195 patients with carcinoma of the stomach, the operability was only 22 per cent That this is not unusual is evidenced by the fact that in the discussion of a recent paper on this subject read by Lahev before the annual meeting of the Pennsylvania State Cancer Society. a good sized clinic functioning in a rural section where patients do not seek early investigation for gastric discomfort, reported their operability as only five per cent and another group as seven per cent It will always be true that where the operability is low, the curability will be low and the mortality high

There are features about carcinoma of the stomach which will make early diagnoses persistently troublesome and a high percentage of cures difficult to at-The fact that gastric carcinoma tends to diminish gastric acidity rather than increase it, brings about gastric comfort rather than the distress which is associated with high gastric acidity The type of carcinoma peculiar to the stomach and the caliber of the stomach are such that when obstructive symptoms occur, similar to those warning symptoms present in distal colon cancer, the lesion is frequently so far advanced that it is inoperable Similarly gross hemorrhage is so rare in carcinoma of the stomach that as a symptom it has almost no warning value Persistent occult blood in the stools, on the contrary, is quite a consistent feature of carcinoma of the stomach and a diagnostic measure all too infrequently used in patients under suspicion for this lesion.

Add to these features the fact that the stomach has such a rich supply of lymphatics, that it is constantly subjected to powerful peristaltic waves well calculated to disseminate malignant cells, that it has an extremely rich blood supply, and that it is partly hidden under the costal margins, making palpation of early lesions here difficult, and it at once becomes obvious that to make earlier diagnoses of cancer of the stomach is going to require earlier and more frequent x-ray examinations upon relatively intangible evidences and suspicions of the presence of this disease

One not infrequently hears and reads that the way to improve our results in cancer of the stomach is to submit all gastric lesions to radical surgery, in order that a carcinoma may not be overlooked and in order that malignant degeneration of the gastric ulcer does not occur This is, Lahey believes, a wrong attitude, and were it employed on a large scale, the operative mortality would at least approximate, if not surpass, the percentage of gastric carcinomas which are missed under the plan of preoperative segregation by frequent x-ray observation while under a short period of hospital observation under medical management

More and more gastroenterologists and surgeons are coming to believe that the percentage of malignant degeneration (if such a condition really exists or the lesion is a malignancy from the start which has ulcerated) is quite low, five, six or seven per cent. The entire question of the percentage of malignant degeneration of gastric ulcer is open to great possible error, not only in the preoperative decision but also as to the microscopic diagnosis of malignancy.

What one's attitude should be toward all gastric lesions is that they must all be suspected of malignancy and that unless these patients can be made symptom free by nonoperative measures, and all x-ray evidences of the gastric lesion made to disappear completely, then they must fall into the group of probably carcinomas of the stomach, and radical surgery and its attendant risks accepted as justifiable.

What is obviously most needed in carcinoma of the stomach is earlier diagnosis. To accomplish this, the physician must submit his patient, particularly when he is more than 30 years of age, to bismuth, x-ray and fluoroscopic examination of the stomach, whenever digestive symptoms persist beyond a week's time Patients of this age or past must not treat digestive disturbances lasting over a week by means of the various advertised indigestion remedies; they must seek advice with the definite idea in mind that, if indigestion has persisted for more than a week or repeatedly recurs, they should be examined to determine if the lesion is malignant

As Lahey has said before in discussing this subject, if we are to discover gastric cancer earlier, doctor, and patient alike, must understand that in a great majority of cases the x-ray examination for gastric cancer will be negative so that rather than be critical of the expense to which he has been put for x-ray examination, the patient should be thankful that his doctor has taken such precaution, doubly so when the findings are negative but even more appreciative when the doctor's wise forehandedness has made early diagnosis possible and he is thus offered a chance of being cured

Because so many patients with cancer of the stomach come for operation late, the end results as relates to cures are

poor, and the general attitude on the part of the surgeon and physician toward this lesion is depressingly pessimistic. One has but to look back a few years on carcinoma of the rectum to recall how pessimistic and depressing was the attitude of patient and doctor, how low the operability, and how high the operative mortality This has now been gratifyingly changed Of Lahey's patients with cancer of the rectum who have had the radical operative procedure, 46 per cent are alive and well over five years The operative mortality has fluctuated with operability from eight to 12 per cent and the operability has increased in the last two years from 54 to 70 per cent

From the point of view of operability, operative mortality or curability, cancer of the stomach, for the reasons given herein, will never be as satisfactory a lesion to treat as cancer of the rectum, results can be greatly improved, however, in fact, much of the improvement has already been made

Many surgeons in this country have acquired experience and skill with the operation of partial gastrectomy, and with the recent advances which have been made in the production and maintenance of anesthesia, a surgeon can do this operation with greater case for himself and with greater safety for the pament. Improved diagnostic measures are also available for early diagnosis. One pressing need remains, however, to secure improved results in this field, and that is the opportunity to make earlier diagnoses so that the advances in gastric surgery may be applied in the early stages of the lesion when better chances of cure can be offered. All the groundwork for improvement in this field has been accomplished except the education of the public to refrain from self-treatment of indigestion and to submit to early and complete investigation in the presence of gastric distress and discomfort.

Curability of Carcinoma of Stomach-V. C. Hunt¹⁰³ believes that the present status of operability of carcinoma of the stomach is that in about 50 per cent of the patients the disease is clinically inoperable at the time the diagnosis is established Clinical inoperability in these cases may be manifested by ascites, fixation of a large palpable mass, laundice, or definitely palpable metastatic involvement Carcinoma in its various situations in the stomach differs greatly in its clinical manifestations and in its curability As there is no clinical syndrome by which early carcinoma of the stomach may be recognized, competent roentgen investigation of the gastrointestinal tract will reveal early operable carcinoma more frequently than heretofore and will materially enhance the possibility of cure Once the diagnosis of carcinoma has been established and no clinical evidence of remote or metastatic extension of the disease is discernible. surgical exploration promptly becomes urgent Progress in the curability of carcinoma of the stomach will not occur through extending the limits of operability and the execution of more radical surgical procedures for extensive disease However, opportunity does exist for enhancing the curability of this disease through submitting the patient to the highly perfected methods of establishing gastrointestinal continuity early after the inception of the disease when it is still closely confined as an intragastric lesion For improvement in the present outlook in carcinoma of the stomach the patient is not dependent as much on the surgeon as on the physician from whom he first seeks counsel

Prognosis—According to D C Balfour¹⁰⁴ the curability of cancer of the stomach by surgical removal of the

growth has been well established When the growth and the regional lymph nodes can be thoroughly extirpated five-year cures in about 30 per cent of the cases. This figure is based on 18 per cent of five-year cures when the lymph nodes are involved, and 48 per cent of five-year cures when they are not involved. In view of the absolute hopelessness of the disease when treated by any other method, the importance of developing every means of recognition while the growth can yet be removed should be emphasized

Accuracy in the prognosis of disease is properly interpreted by the layman as an evidence of professional experience and knowledge When the condition is moperable, any information which can be given as to the expectation of life, the nature of the symptoms which probably will mark the course of the disease. and what can be expected from the treatment of these symptoms is most gratefully received Also, in those cases in which the growth can be removed, or some palliative procedure can be carried out, the family should be informed of the facts on which the prognosis is based

The findings reported here, as related to the prognosis, are based on a series of 4793 cases of gastric carcinoma in which operation was performed at The Mayo Clinic in the period from 1906 to 1931 In 2112 of these cases the growth could be removed either for palliation or in the hope of cure. The expectation of life in the group in which exploration revealed the disease too advanced for either gastric resection or gastroenterostomy was five months In the group in which gastroenterostomy was performed, the expectation of life was only one month more, or six months, and the mortality relative to the operation was 11 per cent

In the cases in which the growth was removed, the hospital mortality was 13.9 per cent. A low mortality is chiefly dependent on proper preparation of the patient for operation and meticulous attention to all those details which lessen the likelihood of development of the two chief causes of death in such cases, namely, peritonitis and pneumonia.

Many factors may be taken into consideration in estimating the prognosis when the growth can be extirpated, namely, the age of the patient, the duration of the symptoms; the gastric acidity; the size, situation, and extension of the lesion into the serosa, and lymph nodes, and the pathological characteristics. Although some of these factors prove to be of little significance, they are at least interesting, and contribute to a better knowledge of the basis of prognosis.

In so far as age is concerned, it was shown in this series that the percentage of five-year survival in the disease was higher among the older patients, 33 per cent in the age group from 45 to 54 years as contrasted with 25 per cent in the group from 35 to 44 years old

The length of history disclosed the interesting fact that five-year survivals were more frequent among those cases in which gastric symptoms were of longer duration, for of the patients whose symptoms had been present for 12 months or more, 35 per cent lived five years, while of those whose symptoms had been present for six months or less, 25 per cent were alive and apparently well, at the end of five years

The investigation of survival based on the size of the lesion disclosed the curious fact that there was greater expectation of life among patients who had the larger lesions than among those those who had the smaller lesions. This is probably attributable to the fact that

the smaller lessons are more likely to be of a penetrating character and also of a higher degree of malignancy than the larger lessons

The situation of the lesion is of significance, and in this series the observations of others are confirmed The observations referred to are, namely, that the nearer the lesion is to the pylorus, the more difficult it is to cure, and that removable lesions in the body of the stomach are accompanied by a distinctly higher rate of survival (40 per cent) than those near, or involving, the pylorus (28 per cent) This may be attributable to the fact that regional lymphatic structures are more easily removed with thoroughness when they are in the former situation than in the latter. and also to the fact that not enough attention has been given to the importance of removing a segment of the first portion of the duodenum. It has been shown that although gross involvement of the duodenum is exceedingly rare in cases of cancer of the stomach, microscopic invasion can be demonstrated quite frequently

The extension of the lesion has great significance in the prognosis. Five years after operation for cancer of the stomach, is has been noted earlier, 18 per cent of the patients whose lymph nodes are involved and 48 per cent of those whose lymph nodes are not involved are alive. The difference is 30 per cent.

The most accurate prognostic information obtainable in this series proved to be the grading of malignancy by the method of Broders, in which the degree of cellular differentiation is recorded as of Grades one, two, three and four Of the patients with carcinoma of Grade one, or two, 63 per cent were alive five years after operation, and 55 per cent were alive ten years after operation. Of the patients with carcinomatic of the patients with carci

noma of Grade three or four, only 20 per cent were alive five years after operation. These results again substantiate the fact that grading of malignancy stands first in importance in the prognosis

The co-ordination of these various factors added definitely to the accuracy in prognosis at the Clinic Also, this investigation has supported the contention of surgeons that the surgical treatment of cancer of the stomach can and does accomplish more than is recognized, and that constant repetition of this fact is the best means of effecting earlier recognition of the disease

Total Gastrectomy - Total gastrectomy offers the only curative measure for cancerous lesions involving a large part of the stomach Its scope of application is, however, decidedly limited Howard M Clute and Hollis L Albright 105 state that relatively few cases of extensive malignancies of the stomach present conditions sufficiently favorable to permit undertaking such a radical procedure, the operation itself is attended with major risks, and the experience of operators in general has shown that the procedure is associated with high mortality. Yet, because in an occasional case offering favorable conditions, total extirpation of the stomach has afforded the patient several years of life with comfort, the operation must be recognized as holding an important place in the treatment of extensive cancer

Operative Technic—The important steps in the operative technic are as follows

- 1 Abdominal exposure
- 2 Exploration of the abdomen
- 3 Determination of operability of the growth
 - 4 Division of the duodenum
 - 5 Freeing of the stomach

- 6 Anastomosis of the esophagus and jejunum.
 - 7 Closure
 - 8. Provision for early feeding

General Consideration—Case Selection—The first consideration must be the general condition of the patient. A person who is thin and preferably under 50 years of age is the ideal case. One of the writers has carried out his most

reports in literature have shown that favorable results have been obtained from total gastrectomy performed for several different types of cancer. The linitis plastica type of growth lends itself best to operation for several reasons. Although growth is extensive, it develops mostly at the pylorus, leaving the cardiac end free, and it is less likely to be complicated with distant metastases.

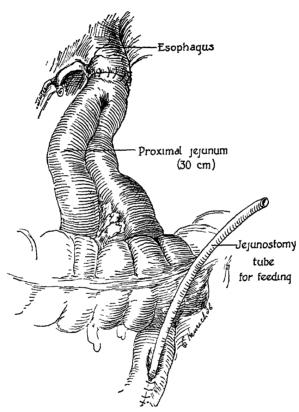


Fig 66—Esophagojejunal anastomosis completed. Lateral anastomosis of the jejunal loops not necessary in the retrocolic operation. A jejunostomy for feeding is a desirable addition (Courtesy, Am. J. Surg. Jan., 1937.)

successful total gastrectomy in one such patient, who was a woman of slender build, about 36 years of age. The fat, plethoric patient, on the other hand, does not withstand the operation well, and the technical difficulties encountered in carrying out the procedure in this type of patient are great.

As to the influence of the type of growth upon the success of the operation,

The operation is definitely contraindicated in the presence of metastases to the liver. In cases with metastases to the omentum, when the involvement is not too extensive the operation may be performed successfully, but the advisability of its use in these cases is always to be questioned.

Preoperative Care—Most of the patients who seek relief are in poor condi-

tion, they are anemic and weak, and the kidney function may be disturbed from lack of fluids *Blood transfusions* should be given for the anemia a day or two before the operation. *Glucose* and *fluid administrations* will improve the kidney function and provide for some restoration of the liver function

Postoperative Care — Morphia is used to control pain, but care should be taken to avoid interference with respiration by administering too large doses of this drug.

The fluid intake is maintained by an intravenous administration of ten per cent glucose solution in 750 to 1000 cc of normal salt solution once a day, and by subcutaneous administration of 1500 cc of saline solution once a day Because of the discomfort caused by the subcutaneous administration, this is done in the morning, and the intravenous is given at night

If there is a jejunal tube in place, the Murphy drip apparatus may be used, and drops of peptonized milk and water are continuously passed into the jejunal tube at the rate of 30 to 40 a minute

If there is vomiting, distention or disticss, a Levine tube is passed and lett in place in the jejunum

After four or five days sips of lukewarm water are given by mouth for 24 hours. Then, a thin gruel of oatmeal or cream of wheat, an ounce or two an hour, and water are given, followed by a soft diet of milk toast, custards and cream soups After ten days a semisolid diet may be taken without difficulty For a time the patient continues to eat five small meals a day but gradually he adapts himself to normal regular eating

End Results—From the standpoint of the duration of life, it cannot be said that the results of total gastrectomy are gratifying Death has occurred in many cases from recurrence or metastasis. When there has been no recurrence, the development of anemia seems to have been the factor responsible for death. The longest period that a patient has lived, according to reports in medical literature, is four years and eight months. This was a case reported by Zikoff Mayo's patient lived four years.

From the standpoint of restoring health to the patient for a period of several months or years, the results of this operation are decidedly favorable. The patients have good appetite, they enjoy eating, and the disturbances subsequent to the operation may be controlled sufficiently to avoid discomfort. Some patients are able to resume their occupations and lead active lives. One of the writers' cases lived three and a half years with comfort and was able to return to her work.

PERITONEUM

By Francis L Zaborowski, MD

OMENTUM

Experimental Pathology of Torsion of the Greater Omentum

I Scalone¹⁰⁶ found that torsion of the omentum produces anatomical and functional disturbances of the various abdominal organs, from traction and interference with the circulation. The torsion of the omentum forms a very favorable focus for the development of any bacteria that may be in the blood

Of the six animals inoculated with bacteria, while they had torsion of the omentum, four died within a few days and the others suffered very severely

PERITONEUM

Pseudomyxoma of the Peritoneum of Appendicular Origin

Péan in 1871 described this condition as "gelatinous disease of the peritoneum" and believed it to originate from the peritoneal serosa

Etiology—The condition seems to occur most frequently after the thirtieth year of age It may develop from the rupture of a sterile, appendicular hydropic mass. The rupture is usually caused by trauma and is rarely the result of an infectious ulcerative-necrotic process. The gelatinous masses may be whitish, amber, yellow, or gray They are usually acellular, but in some cases may contain lymphocytes, erythrocytes, and stellate cells of the connective tissue type As a rule they are sterile, but some investigators have reported the presence of bacterium coli The symptoms are not specific Differential diagnosis is made from appendicular abscess, true neoplasms, and ovarian pseudomy soma The roentgen findings are misleading

D Soh¹⁰⁷ reports a case in a man 42 who for three years had suffered from gastric disturbances. One day, while riding in an auto he was severely jarred and developed a severe pain in the cecal fossa. At operation the appendix was found hydropic, rigid, and markedly dilated. Histologic examination of the appendix revealed essentially mucous degeneration of the wall along its entire length.

Prevention of Peritoneal Adhesions

Ochsner and Storck¹⁰⁸ report 231 cases in which papain solution was used to prevent the reformation or initial formation of peritoneal adhesions The period of observation following the division of adhesions and use of papain was one year or longer in 82.1 per cent In 37 cases laparotomy was repeated following the use of papain In 22 of these cases there were no adhesions in the abdomen, although many and massive adhesions had been present prior to their division and to the use of papain; in 13 a number of adhesions were present, but many less than before its use, whereas, in two there was a reformation of many adhesions.

Free Gas in Peritoneal Cavity

Free gas can be demonstrated roent-genologically as early as five hours after perforation (Petrén¹⁰⁹) Roentgenologic examinations of patients presenting symptoms of acute abdominal disease demonstrated the presence of free air in the peritoneal cavity in about two-thirds of the cases of perforation of gastric or duodenal ulcer. In about ten per cent of the cases of perforation of ulcer the diagnosis may present difficulties, and in these the roentgenologic demonstration of free gas in the peritoneal cavity is of determining value.

Massive Spontaneous Intraperitoneal Hemorrhage

In the female the likeliest source of hemoperitoneum, occurring spontaneously, are the pelvic viscera, especially the ovaries and tubes. In the male the most common source is one of the mesenteric vessels. A systematic search for the bleeding point should be made, as ligation greatly increases the chance of survival Massive spontaneous intraperitoneal hemorrhage is occasionally en-

countered as a sequel to trauma, in malignant disease, and in ectopic gestation 110

Perforation of Gastrointestinal Tract

It has been observed that fasting animals withstand experimental perforation better than animals which recently have taken food Bergh¹¹¹ and his coworkers established perforations at various levels of the gastrointestinal tract of 145 laboratory animals. There appeared to be no relationship between the location of the perforation in the wall of the stomach and the develop ment of peritonitis Perforation of the stomach containing food was performed in 30 animals, with a mortality of 867 per cent. Perforation of the duodenum was established in 16 dogs, with a mortality of 812 per cent from peritonitis l'erforation of the jejunum at various distances from the duodenojejunal angle was carried out in nine dogs, with a mortality from peritoritis of 44.4 per cent. Perforation of the lower ileum was performed in nine dogs and all died from peritonitis within 72 hours. Of seven dors in which the cecum and descending colon was perforated, two died in each series. Perforation of the rectum through the anus was performed on eight animals and only one died. In the seven where the mersion healed without the termation of adhesions

Peritonitis and Gastrointestinal Surgery

The human peritoneum has great resistance to bacterial contamination as evidenced by the prompt recovery after the removal of a gangrenous appendix or after unavoidable soiling when the intestine is opened at operation Fatal peritonitis usually results from massive soiling, extremely virulent bacteria and prolonged inoculation. In 23 cases of fatal

peritonitis reviewed by Shambaugh,¹¹² five were due to a grossly leaking anastomosis, three to a perforation through a carcinoma, one to an open appendiceal stump, one to a slough caused by a tight suture, one to tearing out of a eccostomy tube, five to gangrenous intestine caused by impaired blood supply, one to a fulminating wound infection involving all layers of the abdominal wall. In the other six cases, the fatal peritonitis was caused by contamination of the peritoneal surface at operation

Influenzal Peritonitis

Uebermuth¹¹³ observed a case in which the clinical manifestations were those of an advanced ileus. Operation disclosed a diffuse suppurating peritonitis with subserous focal hemorrhages. These aspects, together with leukopenia, conjunctivitis, initial diarrhea and the development in the course of an influenza epidemic, led to the diagnosis of influenzal peritonitis. The differential diagnosis is difficult, laparotomy is advisable whenever there is the least doubt.

Pneumococcic Peritonitis

W H Cole¹¹⁴ studied 26 cases and deduces that the development of peritonitis secondary to infections such as those of the upper part of the respiratory tract is more common than any other mechanism in pathogenesis Pneumococcic peritoritis is a common complication of nephrosis. In differentiating from acute appendicitis, one notes early fever, profuse vomiting, diffuse character of tenderness and pain and prevalence in guls Diagnostic puncture of the abdomen is justifiable in children when diagnosis Immediate operation is is uncertain contraindicated If the child survives the acute stage, recovery is almost certain, provided the localized abscesses are properly drained

Tuberculous Peritonitis

Tuberculous peritonitis is secondary to tuberculosis of some other organ or tissue. The most frequent sources are the lungs, the peribronchial and mesenteric lymph nodes

Symptoms—The onset of tuberculous peritonitis in children is often stormy, with acute abdominal pain and high fever Differential diagnosis is made from acute appendicitis, abdominal typhus and diplococcus peritonitis in girls

Diagnosis—N V Shvarts¹¹⁵ attaches much importance to the study of the peritoneal fluid obtained by paracentesis. High specific gravity, high albumin content and the presence of lymphocytes differentiate an exudate from a transudate. The Gohn-Lowenstein method of culturing the peritoneal fluid on the newer mediums, such as the Petrignani milk egg medium, yields a much higher number of positive results in finding Koch's bacilli than the older methods

Treatment—General hygiene of the chimatic-sanatorium type with heliotherapy and quartz lamp is preferred Operation is indicated in the exidative torm and in the adhesive and ulcerative-cascating types when signs of increasing intestinal obstruction, of an acute peritoritis due to perforation of the intestine are present. The author noticed no tavorable results with pneumoperitonium and tuberculin treatment.

Fibrous Encapsulating Peritonitis

Etiology—It appears in some cases to be of a tuberculous nature Various authors have added diplococcus infection, rheumatism, typhus, malaria, chronic constipation leading to coprostasis and alterations in the serosa, acute enteritis with lymphatic extension to the serous surfaces of the intestine, and anomalous reaction of a constitutional

nature to various infectious accidents within the abdominal cavity. N. L. Blumental¹¹⁶ reports three cases and collected 63 from the literature. He believes that *polyscrositis* is a local manifestation of a general disease of unknown nature

Diagnosis—This should be based on manifestations of chronic intestinal obstruction with periodic exacerbations, characterized by only moderate distention of the abdomen and absence of a stormy peristalsis and the presence of a swelling and of loud intestinal sounds

Treatment—The operative treatment consists in decapsulation and freeing of adherent intestinal coils. The postoperative period is characterized by manifestations of shock and intestinal paresis and should be combated by subcutaneous and rectal infusions, blood transfusions and administration of cardiac stimulants.

Biliary Peritonitis Without Perforation of the Bile Passages

Etiology—This condition can occur at any age, but is most frequent in from the fifth to seventh decades Women predominated in 116 cases of diffuse and nine cases of circumscribed biliary peritonitis reported by T Batkiewicz 117 Gallstones were present in 60 per cent of the cases. The ductus choledochus and the papilla were totally occluded in only ten cases Dilatation of the ductus choledochus was produced by a new growth in the head of the pancreas or papilla in three patients Eighty-nine patients gave a history of abdominal pain for months or years, but only 13 had typical attacks of gallstone colic Bile may pass through the wall of the gall bladder and has been found in the gall bladder wall In 1917, Blad was able to produce injury of the wall of the gail bladder with a resulting leakage of

bile by introducing pancreatic secretion (trypsin) into the gall bladder In order that the pancreatic secretions may enter the bile passages directly, it is necessary that the papilla of Vater be occluded and that the communication between the excretory ducts exit above the papilla If such a passage should occur climcally, by mechanical obstruction from a stone or a tumor and without the occlusion of the papilla of Vater, the occurrence must be attributed to spasm of the sphincter of Oddi In the absence of gallstones, such a spasm of the sphincter may be produced by inflammation of the gall bladder or bile passages, or even reflexly from other organs Clinical studies showed that in a high percentage of cases trypsin was present in the gall bladder without producing any acute symptoms in the biliary system, apparently the activating effect of bacteria, of cellular degeneration, and of leukocytes is also required

Experiments upon rabbits and dogs showed that the wall of the gall bladder becomes permeable under the action of the pancreatic ferments only if retained bile or infection is present simultaneously

Symptoms—Preceding the onset of the disease there are attacks of pain in the epigastrium or definite gallstone attacks The symptoms of biliary peritonitis usually set in suddenly with pains in the right hypochondrium, in the region of the liver and the stomach. They reach their acme in two or three days and then radiate further, sometimes throughout the entire abdomen The pain is increased with pressure, sometimes sensitivity to pressure is greatest in the right lower quadrant and is mistaken for acute perforative appendicitis Vomiting is frequent. The temperature is elevated early and drops as the condition advances The pulse is accelerated The

abdomen is distended and the abdominal walls are tense There is obstipation. The symptoms develop more slowly than those of ordinary peritonitis. In cases with nondiffuse, encapsulated exudate the general symptoms are less pronounced while the local symptoms are more sharply limited.

Differential Diagnosis—In the majority of cases a diagnosis of acute pertonitis resulting from appendicitis is made. In others a perforated gastric or duodenal ulcer is assumed. It is difficult to exclude acute pancreatitis or gallstone colic with localized peritonitis or peritonitis due to perforation of the gall bladder or the bile passages.

Treatment-In the presence of encapsulated exudate the abdomen is opened and drainage instituted In diffuse biliary peritonitis a perforation should be looked for In severe cases, if a perforation cannot be found, cholecystostomy with drainage of the area about the gall bladder should be done If the patient's condition is good and gall-stones or definite injury to the gall bladder wall is found, a cholecystectomy is done with drainage papilla is occluded, a choledochotomy and dramage is done first, the lumen of the papilla is re-established sometime later Of the 113 cases collected by the author, the mortality was 32 per cent

Pathology—The microscopic and histologic signs of the removed gall bladder as reported by G Scoppetta¹¹⁸ showed that the structure is enlarged, edematous and thinned walled, especially at the fundus The mucous membrane is hemorrhagic, and ulcerated Microscopic examination shows absence of the epithelium of the mucosa, fibromuscular destruction and infiltration, formation of microscopic abscesses, changes in the blood vessels and inflammation and necrosis of the

walls of the gall bladder, most intense at the areas of thinness of the structure

Biliary Peritonitis with Spontaneous Rupture of the Bile Ducts Under Glisson's Capsule

Etiology—Toldt first described large subserous bile ducts, the dilatation of which, with simultaneous atrophy of the surrounding hepatic tissue, may result in rupture of these ducts with discharge of bile into the abdominal cavity. As the result of disappearance of the hepatic tissue, these ducts lose their physiological support and their specific function and are drawn nearer Glisson's capsule, and as the consequence of considerable stasis they swell and rise under the serosa

J Måsek¹¹⁹ reports a case in a man 66 who was suffering from jaundice due to a cancer of the papilla of Vater Later he developed a feverish condition with painful swelling of the gall bladder and the left lobe of the liver. A few days before death, sudden collapse of the previously enlarged and easily palpated gall bladder and left lobe of the liver occurred with severe pain resembling that of stone colic

PANCREAS

Surgical Conditions

Diagnosis—The most important clinical symptom in pancreatic disease is pain which is due to local irritation of the nervous elements within the gland itself. The various radiations of the pain are probably related to the site of the pathological process within the gland. The demonstration of specific ferments in the serum and urine constitutes a very important aid in the diagnosis. The normal diastase value in the serum ranges from 100 to 300 mg per cent. In determinations of the atoxyl-resistant.

lipases in 214 normal cases, T. M. Beckman120 found that this fraction may increase in the serum in conditions such as advanced cachexia, pernicious anemia, endocrine disturbances, thyrotoxicosis, certain arthropathies, however, atoxyl-resistant lipase may be regarded as specific for the pancreas In acute pancreatic necrosis, diastase is already demonstrable from six to eight hours after the onset and disappears within two or three days whereas the lipase level usually increases after two or three days In carcinoma of the pancreas the values of diastase and lipase rise above normal in about half the cases L S Fallis¹²¹ believes that the extreme rarity of Cullen's sign suggests an anatomic variation of the structures at the um-Effusions of blood resulting bilicus from disintegration of the gland could conceivably track around in the subperitoneal space between the peritoneum and the transverse fascia and, reaching the midline anteriorly, would be limited by the suspensory ligament of the liver above and the urachus below the umbilious, coming in contact with the subcutaneous tissues owing to the absence of the transverse fascia in this region

R Elman¹²² made blood amylase determinations according to the method of Somogyi, in eight cases of acute epigastric pain and found it to be high at the height of the attack and gradually declining following subsidence of the symptoms. Out of a group of 141 patients, J. W. Grott¹²³ found pancreatic diastase in the urine was increased in 44 cases In determining the pancreatic diastase, freshly eliminated urine is used because the amount of diastase diminishes by exposure. A. Mahner 124 reporting on 19 cases of acute pancreatitis found no parallelism between the diastase content and the severity of the case. He found a high diastase content in the urine of

mild cases and a much lower content in some of the severe cases On the other hand, increasing diastase content of the urine is proof of an organic disease of the pancreas. The author uses Wohlgemuth's method for determination of the diastase content of the urine in acute pancreatitis and in the chronic cases, the Rona and Michaelis serum lipase re-Paul's review of 23 cases of carcinoma of the pancreas shows that. while a majority give some evidence of the presence of the neoplasm when studied by means of a barrum sulfate meal, this evidence is often difficult to evaluate and may even be misleading, since the diagnosis depends mainly on the secondary effects of the tumor on the stomach and duodenum

Acute Pancreatitis

Treatment - Immediate operation is done to evacuate fluid, clots, and necrotic masses, and to decrease the presence of bile in the ampulla of Vater. If the pancreas is not necrotic, a cholecystostomy is done and the peritoneum drained by tube or agaret drain. The pancieas is not disturbed If the pancreas is hemorrhagic and slightly necrotic, gauze drains are carried to the overlying peritoneum, cholecystostomy done, but the pancreas If the pancreas is is not disturbed necrotic, hemorrhagic or suppurating, the adjacent peritoneal cavity is temporatily walled off by gauze packs, clots, pus, and necrotic sloughs evacuated, and drainage instituted with tube or cigaret drains through the incised gastrocolic omentum and through a stab wound in the left costovertebral angle

In the preparatory and after treatment calcium, glucose with insulin and Ringer's solution is used freely. For traumatic rupture of the pancreas, prompt exploration, with ligation, suture, pack or drain to protect the adjacent tis-

sues from the erosive pancreatic secretion is done 125

H Wildegans¹²⁶ reporting on 32 cases of acute pancreatic necrosis, delayed operation in 28 cases purposely, and four to eight weeks later did a cholecystectomy with common duct drainage in 14 cases, with 14 recoveries. Of the entire series of 32 cases, five died

Chronic Pancreatitis

Treatment—The treatment of *chronic* pancreatitis is often a long drawn out procedure, all irritating foci of infection should be removed. Ten units of *insulin* once or twice a day is important.

P Mallet-Guy^{1,2,7} reports three cases of chronic pancreatitis localized in the body of the gland for which a left hemipancreatectomy was done in one case and partial pancreatectomy with cholecystostomy in two others

Partial pancreatectomy in convulsive states associated with hypoglycemia is advised by J. M. McCaughan and G. O. Broun 128 From a study of case reports in the literature it is evident that the end results of operations in cases with islet cell tumors are excellent, and in cases without adenomas the results are gratifying. The author's results in their cases of hypoglycemia with nervous manifestations were very disappointing S F Herrmann and John A Gius¹²⁹ report a clinical cure of a case hyperinsulinism of a marked degree associated with a pancreatic calculus The calculus was in the head of the pancreas and no pancreatic tissue was removed

Acute Pancreatic Necrosis

Etiology — In 1278 operations for acute pancreatic necrosis collected by Schwiedey, stones in the common duct were found in 194 per cent of the cases and in the ampulla of Vater in 63 per cent. The great frequency of cholelithin-

asis and the great rarity of pancreatic necrosis suggests that they do not stand in causative relationship to each other. P D Solovov¹³⁰ believes that acute pancreatic necrosis is a hyperergic inflammation in an organism previously sensitized by some allergen. Trauma, especially surgical trauma, often gives rise to pancreatic lesions. Other etiologic factors are biliary stones, infections of the biliary passages, and duodenal ulcers. Since the gland undergoes continuous changes any irritation is capable of producing a large number of different morbid conditions.

Traumatic rupture of the pancreas as the only lesion is rare and presumably occurs, when the stomach is empty, through pressure of the pancreas against the spinal column by the object struck.

Pancreatic Carcinoma

Etiology-E Wetz131 reporting on 32 cases found it more common in males than temales. The average age of the patients was 55 years. Among the factors to which the condition has been attributed are alcoholic abuses, gastric ulcers involving the glands, developmental anomalies and aberrant germ buds of the pancreatic ducts, pancreatic curhosis, gallstones and chronic cholecystitis. The head of the pancreas is most frequently involved. Hoffman concluded that in the United States about 4000 people die of carcinoma of the pancreas each year. The cancer may originate in the epithelium of the efferent ducts, in the parenchyma of the gland, or rarely in the islands of Langerhans Metastases take place early

Symptoms and Diagnosis—The occurrence in a man at middle age of digestive disturbances, epigastric fullness and discomfort, pain and weight loss warrants a thorough study by all means available If no other condition is re-

vealed by examination and gastrointestinal studies, the possibility of pancreatic cancer must be considered at once. Emaciation, nausea, vomiting and copious fat stools containing undigested fat and muscle fiber or other interference with the pancreatic secretion occurs. Jaundice is persistent and complete, the stools are clay colored and the urine dark. In carcinoma of the pancreas the blood-sugar curve rises rapidly and falls slowly. The prognosis is unfavorable

Treatment-High voltage roentgen therapy appears to be the least valuable type of therapy for cancer of the pancreas Very possibly a two-stage operation in which a biliary intestinal anastomosis is done in the first stage and two or three weeks later, radium is implanted in the second would be However, in cancer of the destrable pancreas simple exploration has a definite mortality and the average length of life after exploration is less than if no operation was done Patients with pancreatic cancer are prone to develop later difficulties from infections of the biliary tract from the anastomosis

Fistulas and Cysts of Pancreas Following Operations for Hyperinsulinism

Whipple¹³² reported the occurrence of pancreatic fistulas in 3 of 35 operative cases or 85 per cent. F. N. Allan, W. C. Boeck, and E. S. Judd¹³³ reported one case of pancreatic fistula following partial resection of the pancreas in a patient without pancreatic tumor. After resection, clamps had been left on the remnant of the body and according to these authors, a fistula developed in each case after the clamps were removed. E. S. Judd, F. N. Allan, and E. H. Rynearson¹³⁴ reported two more cases. One developing after the excision of a cystic tumor, the other case

following a partial pancreatectomy where no tumor was found N A Womack, W. B Gnagi, Jr, and E. A Graham¹³⁵ report a case following the dissection of an adenoma J M McCaughan and A. A. Werner 136 report a case of pancreatic fistula and cyst which developed following the removal of a small wedge of pancreatic tissue which had been devitalized and traumatized by the holding The excision of pancreatic tumors by the removal of a surrounding wedge of normal tissue appears to be a more likely cause of fistula than does partial pancreatic resection. Infection in these fistulas no doubt takes place from the bacteria derived from the skin about the cutaneous opening of the tistulous tract

Treatment—The wounds usually heal themselves within several months. Occasionally incision and drainage is necessary before healing takes place. If the fistula does not close spontaneously while adequate drainage is being provided its implantation, into the gastromtestinal tract must be attempted.

SPLEEN

Hypersplenia

 $W = Schmidt^{4/37}$ reports the histories of a girl ten, and a boy 14, both of whom had severe anemia with leukopenia and thrombopenia Neither the shape nor the resistance of the crythrocytes was changed and there were no signs of in creased blood destruction in the spleen Nevertheless, he reasoned that if it did not produce anemia by destruction it might produce it by exerting an inhibiting effect on the blood formation in the Naegeli regards hyperbone marrow splema in this light by ascribing the inhibiting action to the endothelium of the splenic sinuses. The connection between spleen and bone marrow supposedly takes place by way of the blood stream, by means of a substance that is formed in the endothelium of the splenic sinuses Splenectomy was followed by a noticeable improvement in the anemic condition and by an increase in the leukocytes and the platelets

So-Called Spontaneous Ruptures of Spleen

Opinions are divided about the spontaneous rupture of an intact spleen Spontaneous ruptures do occur in certain pathologic changes of the spleen, such as exist in malaria, typhoid, leukemic splenomegaly and splenic congestion. The possibility of a traumatic, so-called two-stage rupture, has likewise been generally recognized There is the possibility of spontaneous rupture of a spleen that from the morphologic point of view 15 essentially normal E Ask-Upmark¹³⁸ suggests that in these cases a circulatory disturbance of functional origin may be the cause, which leads to hemorrhage and then to rupture

Splenectomy for Hemoclastic Crises

(r M Curtis, C A Doan and B K Wiseman¹³⁹ performed splenectomy successfully on eight patients during an acute hemoclastic crisis. Six of the patients had congenital hemolytic reterus, two had thrombopenic purpura. The outcome supports the rationale of splenectomy in the treatment of properly selected and prepared patients suffering from hemolytic reterus or thrombopenic purpura of splenic origin.

Splenectomy in Chauffard-Still's Syndrome

M. Loeper and his associates¹⁴⁰ describe a case of polyarthritis with enlarged spleen, lymph nodes and increased temperature. After splenectomy the pa-

tient improved rapidly, functional impairments disappeared and the joints became freer in their movements. Five weeks after the operation there was a sudden onset of bilateral bronchopneumonia, from which the patient died. This splenectomy for Chauffard's polyarthritis is, according to the authors, the third of its kind mentioned in the literature. Both preceding cases were rewarded with permanently favorable results.

A. Splenomegalic Cirrhosis of the Liver

R Brandberg¹⁴¹ reporting on 36 cases found this condition more common in men than women. Two types were distinguished, one was characterized by signs of stasis of the portal circulation, hemorrhages from the alimentary canal and ascites. The liver was reduced in size and not palpable. The splenic enlargement was due to congestion Splenectomy resulted in reduction of the portal blood flow. Liver pathology was unaffected by the operation indeed, where there were serious curhotic changes in the liver, the liver condition progressed and was fatal after splenectomy. Of 21 patients who showed preoperative signs of stasis in the portal circulation only two were benefited by the intervention The second type of liver cirrhosis showed no signs of circulatory disturbance in the Most of the patients were portal flow women of middle age. Chronic infection or intoxication was the chief cause mia, both with and without increased hemolysis, was not uncommon. Seven patients were still living, from 3 to 15 years after splenectomy. When the liver was strongly attacked, it was noted, the spleen was injured to a less extent, and The prognosis was best in the cases without pronounced anemia before operation

B. So-Called Thrombophlebitic Splenic Tumors

In this group of 30 cases, there was obstruction of the portal stream in the absence of liver cirrhosis. Eleven of the patients were under 16 years of age Often cases in which autopsy was done, thrombosis of the splenic vein was found in four and thrombosis of the portal vein with or without associated splenic thrombosis in six. In most of the cases the thrombosis was the primary change and the splenic enlargement occurred secondarily as the result of stasis. In two cases, the hematological changes suggested that the splenic enlargement was primary and the thrombosis secondary The prognosis is better for children than for adults After splenectomy, 12 of the patients died soon after operation, eight died during the next eight years of hemorrhage or intestinal gangrene, one died of a special complication, and one could not be traced Eight patients are living and free from symptoms from 2 to 14 years after the operation Recurrences are common due to the tendency of the thrombosis to recur and progress

C Chronic Infectious Splenic Enlargements

In this group there were 31 cases Twenty-five were women, most of whom were middle aged. Symptoms of stasis of the portal flow were absent. Besides the splenic enlargement, there was anemia and leukopenia, often associated with pronounced granulocytopenia bopenia was sometimes found. In several cases the blood changes disappeared after splenectomy, in others, they were affected little, if at all, by the operation. If the cause of the disease cannot be eliminated, the blood changes persist whether the spleen is removed or not. Several cases showed a distinct tendency toward infection both before and after the splenec-

The cause of the susceptibility to infection is evidently the blood changes, especially granulocytopenia In group, six patients died in the hospital, nine died after leaving it, seven were completely cured, eight were benefited, and one was not benefited. If the extremely enlarged spleen is not removed it may lead to the severe sequelae causing circulatory disturbances of the portal circulation

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INHALATION ANESTHESIA

By HENRY S RUTH, M D.

CYCLOPROPANE

Although six years have elapsed since the first clinical application of this anesthetic agent by Waters, in his usual conservative manner, he believes that it should be considered as still being in the experimental stage. Nevertheless, its use has now become so widespread that it is employed in practically all of the civilized countries of the world Therefore it may now be considered with logic to be an important addition to anesthetic practices

History - Cyclopropane was discovered and described by Freund in 1882 No further studies were made until 1929. in which year Henderson and Lucas first considered it as a possible contaminant of propylene. Upon further investigation of this latter drug, they found that the untoward reactions developing were produced by propylene itself, and that evelopropane appeared to be nontoxic and a better anesthetic agent than propylene Waters, after further laboratory studies, then initiated its clinical application, since which time numerous contributions have been made to its literature from many parts of the world

Chemistry — Cyclopropane may be prepared chemically by two methods (1) The reduction of an alcoholic solution of trimethylene bromide in the presence of metallic zinc, and (2) from propane in natural gas by progressive thermal chlorination (Purdue process) It is a colorless hydrocarbon which is in the gaseous state at atmospheric pressures An isomer of propylene, it has the same chemical formula, C3H6 In contradistinction to propylene, its structural formula shows it to be a saturated hydro-

 CH_2 Its molecular carbon CH₂ — CH₂

weight is 4205, and it has a specific gravity of 146 For clinical purposes, it must be considered an explosive agent, because the anesthetic mixtures ordinatily employed are all well within the explosive range. It liquefies at a pressure of 75 pounds per square inch (34 kg per 64 square cm), under which pressure it is stored in cylinders appears that under average conditions, it can thus be stored indefinitely

Pharmacology—Its absorption from the alveolar spaces by the body tissues is rapid, but it appears that it takes longer for equilibrium to be established between alveolar and tissue concentration than with other anesthetic gases. It is believed that a normal individual is not affected by inhalation of a concentration of less than 35 per cent Nine per cent has produced unconsciousness. Ten per cent is regarded as the average for light anesthesia, and 14 to 16 per cent for satisfactory, deep anesthesia. As with any

inhalation anesthetic, these percentages vary with the individual patient Cyclopropane does not stimulate respiratory function as do the other inhalation anesthetic agents The usual concentrations employed are not irritating to the respiratory mucosa. A very gradual and progressive decrease in depth of respiration occurs below the first plane, third stage level of anesthesia No oxygen want should develop readily, for it is customarily administered with high oxygen concentrations, unless minute volume respiration is depressed to a very marked degree On circulation, the pulse rate is usually normal or but slightly increased Blood pressure is not usually affected unless carbon dioxide elimination, oxygen supply, or respiratory function is interfered with Changes in cardiac rate and arrhythmias occur in the presence of high concentrations. The first disturbance of the pulse is usually a lowering of the rate Later, a tachycardia may develop, or sinus arrhythmias, or ventricular extrasystoles These disturbances rhythm are controlled by lowting of the concentration of cyclopropane by addition of oxygen or air. The metabolic changes produced are slight, there appears to be no effect on liver tunction

Physical Signs — These are similar to those of other anesthesia when cyclopropane is administered slowly, with a tew exceptions. The absence of irritation will allow of a rapidly induced deep anesthesia without the manifestations encountered in the first and second stages when administering irritant agents. Thus, there is a possibility of very quickly establishing a dangerously deep anesthetic level, when this agent is employed by the inexperienced. The most reliable guide concerning the depth of anesthesia appears to rest with respiratory function. Respirations are depressed.

in lighter levels of anesthesia as compared with ether. Pupillary signs are of corresponding less value, particularly in morphinized patients. Constant observation of the rate and character of the pulse, especially immediately after adding more of the anesthetic agent, may also serve to prevent an overdose. Color is of little value, for with an excess of oxygen, little change in color can be noted until respiratory depression is Inflation of the lungs with extreme oxygen is indicated if changes in the pulse occur when respiration is decidedly depressed

Indications—Cyclopropane is exceedingly useful where excess oxygen is of Thus, it has been found useful for thoracic surgery, in hyperthyroid disease, in the presence of respiratory Its ease of obstruction, and anemias induction makes it quite applicable when spinal anesthesia must be supplemented It has also been recommended for use during the course of spinal anesthesia when retching and vomiting are persistent, or when it is necessary to relieve the very nervous and apprehensive patient from consciousness during operations under spinal anesthesia. Favorable results have been most consistently reported after the use of cyclopropane in Cesarean section A smoother convalescence has been noted, presumably because there has been a reduction in the number and degree of postpartum hemorrhages, and there is less disturbance of bowel function. For abdominal surgery, the satisfaction obtained with evelopropane is dependent largely upon the experience of the anesthetist on one hand, and on the demands of the surgeon on the other. For many surgeons, cyclopropane is adequate in the majority of instances. The relaxation obtained with evelopropane, however, is not always satisfactory for a surgeon who has been

accustomed to performing his surgery semiroutinely under spinal anesthesia

Contraindications—The cost of the manufacture of cyclopropane has made its administration by the closed carbon dioxide absorption technic almost mandatory This method of administration, in addition to making the administration of cyclopropane economical, also reduces the possibility of explosions. The explosion hazard is reduced by such a closed system because the gases in the circuit very rapidly become saturated with Its use is contraindicated moisture when the high frequency electrical apparatus or x-ray machines are being employed The actual cautery should not be used in close proximity to the inhaler

Technic of Administration

Preanesthetic Sedation - Preliminary medication may be employed before the use of evclopropane as with other inhalation anesthesias, but not to the same degree because evelopropane does not stimulate respiration. Excessive depressions of respiration during its use may be readily brought about by too heavy preliminary sedation. With the excessive use of the usual sedatives, difficulty may be encountered in obtaining sufficient saturation of the tissues without the use of the dangerous higher concentrations of the gas Morphine, gr 15 to 14 (8 to 16 mg), with scopolamine, $g_1 = \frac{1}{200}$ to $\frac{1}{100}$ (0.32 to 0.65) mg) are usually employed. It has been suggested by Waters that the amount of scopolamine administered may closely approach that which is necessary before other inhalation gaseous anesthetics, but that the dosage of morphia should be reduced

Technic-Induction — Many variations have been suggested, but the most common method is as follows. When the mask is placed upon the patient's

face, sufficient oxygen is rapidly placed in the circuit to more than adequately accommodate the patient's tidal respiration The flow of oxygen is then set at a rate sufficient to maintain metabolic requirements, usually from 200 to 400 cc per minute, and is ordinarily kept at this rate of flow throughout the operation Cyclopropane is added to the oxvgen immediately, at a rate of 400 to 600 cc per minute, depending upon the type of individual to be anesthetized After two to four minutes, the addition of the anesthetic gas can then be stopped completely, or it may be reduced to from 50 to 100 cc per minute A few minutes are then allowed to intervene for distribution of the anesthetic to the tissues The finer adjustments of the later portions of the induction are performed by the gradual addition of the necessary amounts of the anesthetic with intervening intervals to allow for the distribution of the amount added In this way, anesthesia of excessive depth will be prevented and the patient will be gradually taken to the level of anesthesia required for the operation contemplated Cyclopropane is sufficiently potent, so that it is not necessary to wash out the nitrogen in the lungs and tissues of the Therefore, it is not required to empty the contents of the circuit in a well-managed induction

Maintenance — Just sufficient cyclopropane is added in small amounts, preferably at a rate of flow from 100 to 200 cc per minute, or less, as is indicated by the changing level of anesthesia. Greater amounts, of course, will be necessary if there are large leaks present in the system. At the close of the operation, the level of anesthesia may be lightened gradually by the addition of oxygen or of atmospheric air.

Postoperative Results—Waters and his associates have reported a consider-

able lower incidence of circulatory complications with cyclopropane anesthesia than with ether or ethylene, but slightly higher than with nitrous oxide. Clinically, Sise does not believe that there is any higher incidence of cardiac complications than with any other anesthetic agents The respiratory morbidity compares very favorably with other agents Nausea is lessened in major surgery.

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ETHER CONVULSIONS

The problem of convulsions or spasms associated with inhalation anesthesia is one that is presenting itself with increasing frequency. There does not appear to have been any definite reference to this condition in the literature until 1926, and the greatest numbers have been reported within the past few years. The contraction of muscles referred to have nothing to do with true epileptic seizures during anesthesia, but constitute a condition reported upon as "ether convulsions" These have not been limited to the administration of ethyl ether, but among the anesthetics causing them were nitrous oxide, ethylene, ethyl chloride, and chlo-

roform Lundy tabulates 144 cases with a total mortality of 189 per cent. There is a rather loose uniformity in the description of the condition The majority of the patients are children (53 per cent in Lundy's report) or young adults Acute infections associated with high fever appear to be the most frequently The respiraoccurring complications tory rate before the occurrence of the convulsions is usually rapid and may be labored The first indication of oncoming convulsion usually begins with a twitching of the facial muscles around the eyes, which then spreads to those about the mouth. The lids are usually open in tonic spasms The pupils are widely dilated and do not react to light The abdominal muscles begin to twitch and the convulsions spread to the extremities. When the convulsions interfere with respiratory function, evanosis appears. On withdrawal of the anesthetic, the spasms may disappear or remain progressive until a tatality ensues, which fatality may occur on the operating-room table or some hours afterward

The overdose of a local anesthetic into the blood stream is not thought to be identical with the type of convulsion under discussion associated with general anesthesia. As etiological factors, there have been mentioned toxemia and septicenna, impurities in the anesthetic agent, excessively deep anesthesia, instability of the nervous system, overdosage of atropine, heat etc Rosenow and Toyell have suggested that the condition may be mduced by a neurotoxin or poison produced by streptococci in amounts sufficient to cause spasms in the absence of anesthesia, but which may suffice to initiate convulsions during the course of an inhalation anesthetic

Whereas, there appears to be no uniformity of thought with regard to the etiological factors involved, definite rules of treatment can be given. Oxygen must be administered as soon as the convilsions are insufficiently severe to interfere with respiratory function Apneas must be treated by artificial respiration, preferably by means of the introduction of an endotracheal catheter. The convulsions are to be controlled by the intravenous administration of a soluble barbiturate, which may be either sodium pentothal or evipal. One of these should be given in just sufficient amounts to control the convulsions If the convulsions are prolonged so that either pentothal sodium or evipal are not permanently effective, they should be followed by the intravenous administration of sodium amytal or pentobarbital sodium, because of the more prolonged action of the latter drugs

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REGIONAL ANESTHESIA

Epidural Anesthesia

This form of anesthesia has become popular in certain sections of this country within the last year or two. It is a form of block anesthesia which has been employed during the past five years in Europe and South America with apparently good results. It consists of injecting an anesthetic solution into the epidural space Since this space is present only in the vertebral column, the anesthetic solution cannot find its way to the medulla or the brain Anesthesia is accomplished by means of the anesthetic solution, leaving the spinal canal by way of the perineural lymphatics. Thus, the solution bathes each segmentary nerve outside the spinal canal at the point where the nerves no longer retain their dural sheath

Technic-The patient is placed on the side in a position similar to that emploved for lumbar puncture, with the back in the position of dorsal flexion, and with the knees and thighs drawn up to the abdomen, and the head flexed upon the chest. The bowing of the back, which stretches the spinal canal, produces a negative pressure in the epidural space The greater the extent to which the back is bent, the greater the degree of negative pressure is produced. The second lumbar interspace is employed for two rea-(1) It is the widest interspace and (2) it is at this point that the epidural space is the greatest. The back is prepared with an antiseptic solution and An intracutaneous procaine draped wheal is made over the desired space Through this wheal a short beveled spinal needle is advanced very slowly has reached the intraspinous ligament The stilette of the needle is then removed, and a Luer connection, type No 42051, into which has been placed a drop of sterile solution, is attached to the needle. With this indicator in place, the spinal needle is advanced very slowly When the vellow ligament has been transversed a snap is felt, which designates the point of the needle entering the epidural space. If a vacuum has been produced in the epidural space by sufficient bowing of the back, the drop will be seen to move, which movement varies in degree from a slight vibration to complete aspiration of the fluid, depending upon the height of the negative pressure A 20 cc syringe filled with the anesthetic solution is carefully attached to the

needle without changing the latter's posi-Ten cc is then injected slowly. Here the procedure should be stopped for five minutes At the end of this time. if there is no numbness of the extremities and no motor paralysis, it appears certain that the anesthetic solution has not been injected intradurally, and the remainder of the solution can then be injected with A short interval of time should be allowed to lapse between the injections of each 20 cc of solution for purposes of diffusion A total of 35 cc of two per cent procaine is employed for appendectomies, inguinal hernias, and operations upon the lower extremities, 45 cc of the same solution are recommended for gynecological operations, and 50 cc for stomach and gall bladder procedures If the operation is to be performed in the lower abdomen or upon the extremities, the patient should be placed in moderate Fowler's position immediately following the injection, and vice versa, a slight Trendelenburg should be employed when the operation is to include the upper abdomen

The addition of epinephrine does not seem to prolong the anesthetic action Anesthesia lasts for about one hour. For more prolonged anesthesias, 500 mg of procame and 100 mg of pontocame may be dissolved in sufficient physiologic salme solution to make 50 cc. (One per cent procaine and 0.2 per cent pontocame) This solution in the epidural space produces an anesthesia of $1\frac{1}{2}$ to 2 Anesthesia should be hours' duration complete within 15 to 20 minutes after the injection of either procaine or ponto-In unilateral came-procame solutions operations the side to be operated upon should be lowermost during injection

Results—Changes in the blood pressure are usually slight, but there may be a fall of 20 to 30 mm of mercury when high anesthesia is instituted. The

respiration and pulse may increase slightly after the injection. No paralyses have resulted. It is thought to be particularly effective for Cesarean section, as the uterus contracts readily during its use. This form of anesthesia has been suggested also for ectopic pregnancy, gunshot wounds, placenta-previa, and other abdominal procedures in the presence of pulmonary tuberculosis, heart disease, arteriosclerosis, and shock. It is less effective for the neurotic and highly nervous type of patient. Unsuccessful results have been laid to improper technic

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SPINAL ANESTHESIA

Metycaine Spinal Anesthesia

The new regional anesthetic drug, mety-came, is the hydrochloride of gamma (2-methyl-piperidino)—propyl benzoate, and is chemically related to procain and cocain. Compared with procain, it is longer-acting, of approximately the same toxicity when injected subcutaneously, but of increased toxicity when injected intravenously. For infiltration and regional block anesthesia, it is effective more rapidly and surely. It is self-sterilizing and effective by topical application to the eye and urethra

For spinal anesthesia, 2 cc of ten per cent aqueous solution may be employed Suggested dosages of this solution (1 cc represents 100 mg of metycaine) are as follows (dilutions are made with aspirated spinal fluid)

Perineum—04 to 08 cc diluted to 15 to 30 cc

Lower Abdomen—08 to 14 cc diluted to 4 to 5 cc
Upper Abdomen—15 to 20 cc diluted to 5 cc

Woodbridge found the duration of spinal anesthesia 40 to 50 per cent longer than that obtained from procain Two reports (Woodbridge and Tuohy) are based on a total of 1981 cases No fatalities were reported and the incidence of complications directly attributable to the agent was low

Neurological Complications - The literature of the year has taken more cognizance of the neurological sequelae of spinal anesthesia. The more common untoward manifestations of this type of anesthesia, as represented are headache, sixth nerve palsy, aseptic meningitis, and lesions of the cauda equina or conus medullaris. It has also been noted that the symptoms of a latent neurological disease may be precipitated by a spinal Improper concentration of anesthesia the anesthetic solution injected has received most of the onus for these toxic reactions, in that a dilute solution has produced temporary derangements, and concentrated solutions, permanent ones Faulty preparations of the solution have also been suggested as an etiological factor. One case of myelomalacia with fatality was reported, which suggested a possible sensitivity to foreign protein For the persistent headache, the following have been suggested (1) the employment of only small puncture needles, (2) avoiding the loss of spinal fluid during the procedure, (3) patient kept in bed without a pillow for 24 hours, (4) four minimum doses of ephedrine given intramuscularly and repeated two to four times at hourly intervals, (5) 1000 cc of 05 per cent normal saline solution administered intravenously, (6) intravenous typhoid vaccine

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SURGERY OF THE SYMPATHETIC NERVOUS SYSTEM

PAUL G FLOTHOW, M.D.

Introduction — The past year has seen very little that is new in the field of sympathetic surgery. The technic of the various surgical procedures directed toward the sympathetic nervous system has been more or less standardized and, while various new conditions have been treated by sympathetic surgery, in none has the result been sufficient nor startling enough to warrant a great deal of attention. The one subject which has held the continued and increasing interest of those interested in the sympathetic nervous system and its therapy is the surgical treatment of essential hypertension.

Classification of Causes of Hypertension—It is well to call attention to the fact that there are conditions other than essential hypertension which may produce high blood pressure. The following classification is taken from Adson and Allen

- 1 Primary or essential hypertension Estimated 85 per cent of all cases
 - Group 1—Slight to moderate increase in blood pressure, which ordinarily becomes normal as a result of rest Mild sclerosis of retinal arteries
 - Group 2—Moderate to severe hypertension Moderate sclerosis of retinal arteries Occasionally venous thrombosis and arteriosclerotic retinitis

- Group 3—Moderate to severe hypertension Angiospastic retinitis
- Group 4—Moderate to severe hypertension Angiospastic retinitis Edema of optic discs
- 2 Secondary hypertension due to known disease Estimated 15 per cent of all cases
 - (a) Coarctation of the aorta
 - (b) Glomerular nephritis
 - (c) Tumors of the suprarenal glands
 - (d) Hyperthyroidism
 - (e) Arteriosclerosis
 - (f) Traumatic arteriovenous fistula
 - (g) Aortic heart disease

Grouping of Essential and Malignant Hypertensions—While most authorities feel that malignant hypertension is merely an advanced stage of the so-called essential hypertension, there is some disagreement on this point. Some authorities such as Reiseman state that malignant hypertension is a clinical entity and a different disease from essential hypertension. However, for purposes of simplification the cases may be grouped into the following four types.

- Group 1—Benign hypertension, those with slow progression, mild symptoms and only moderately elevated blood pressures
- Group 2—Those with fairly rapid progression, more marked symptoms and greater elevation of blood pressure without marked cardiac, renal or retinal damage

Group 3—Those with moderately rapid progression, moderately severely elevated blood pressure with early retinal, cardiac and renal changes. Early malignant type Group 4—Those with rapid progression, advanced disease, extremely high pressures, marked retinal changes, choked discs and cardiac and renal damage. Malignant hypertension

Essential Hypertension

Surgical Treatment—There are four schools of thought regarding the surgical attack upon essential hypertension, namely, that of the Mayo Clinic, 1, 2 Peet, 3, 4 Crile⁴ and Heuer, 5

In general it may be said that all of the men engaged in this type of work agree that it is far from being a satisfactory answer to the problem of treatment of this condition. The concensus of opinion is, that while it cannot be considered a cure, it is at this time by far the most effective method of treatment, and the work should continue until some better form of therapy is found.

The viewpoint of the surgeon and the internist differs somewhat as to the value of this method of treatment. Internists who have seen only the occasional and frequently the unsuccessful case are very free with their criticism of the procedure Surgeons who have done a great deal of this work, while not entirely enthusiastic about the results are unanimous in feeling that their results render the continuation of this work well worth while Strangely enough, some of the most enthusiastic supporters are internists in institutions where work of this kind is being carried on men who have had opportunity of sceing the cases before and after surgery and of following the postoperative results

The Reviewer has recently visited the Mayo Clinic, the Cleveland Clinic and The University Hospital at Ann Arbor, three centers where a great deal of the

work in this country has been done. He has interviewed both the internists and the surgeons, has inspected the case reports, the follow-ups and the statistical reports of the results of the various types of surgery. It has been an amazing observation that regardless of what the surgical approach has been, and almost regardless of the manner of selection of cases, the results have been very similar in these three different institutions.

The manner of selection of cases varies at each institution. In one a great deal of attention will be paid to a particular point as a criterion of suitability for operation, while in another it will be an entirely different one.

The results are certainly good enough to warrant the continued application of visceral nerve surgery in selected cases of hypertension

Method of Selection — Cases are very carefully selected. They are usually selected by the internist and not by the surgeon. The preoperative studies are made on the medical side, and the internist determines whether or not the neurosurgeon should be offered the case. Very careful preoperative studies are carried out. These include the following.

- 1 Careful examination of the heart including electrocardiographic studies, x-rays and clinical examination
- 2 Careful tests of kidney function including all of the well-known tests, particularly the concentration test
- 3 Careful determination of blood pressure levels with hourly determinations for a period of at least 48 hours
- 4 The determination of the effect of large doses of sodium amytal or nembutal upon the blood pressure levels
- 5 The effect of sodium nitrite on the blood pressure levels.
 - 6 The cold test
 - 7 The intravenous pentothal test.

The age of the patient, the condition of the blood vessels and the duration of symptoms and rapidity of progress are also taken into consideration.

Marked cardiac damage is a contraindication to surgery. However, many
cases of essential hypertension show a
certain amount of cardiac damage, and
it becomes the task of the internist to
determine whether this damage is irreparable. Some cases in which serious
heart complications are present have
shown tremendous improvement after
operation. The estimation of whether or
not cardiac function will improve is a
very difficult one, and rather severe cardiac damage should not absolutely contraindicate the operation, if other factors
are favorable

Severe kidney damage with marked reduction of renal function serves in most cases to contraindicate operation. However, the various tests of renal function do not tell the entire story Peet4 believes the concentration test is of great importance and feels that if the kidneys are unable to concentrate the urine, that operation offers very little hope. When other tests of kidney function such as the various protein tests and the P. S. P. test show marked reduction of function, but the kidney is still able to concentrate the urine, he feels that the kidneys are better than is apparent from the other The presence of albumin apparently is not of great significance with regard to actual kidney function

Allen and Adson2 make the following statements. "We do not consider apparent sclerosis of the retinal arteries, moderate enlargement of the heart, inversion of the T-waves in the electrocardiograms, albuminums, slight reduction in renal function or cerebral vascular accident from which recovery has been satisfactory, contraindications, in themselves, to operation. However, we do not advise

operation for patients who have congestive heart failure, marked renal insufficiency, advanced arteriosclerosis, or angina pectoris."

While the determination of preoperative blood pressure levels is carried out in all institutions, some pay much more attention to this factor than others.

The effect of sodium amytal, 9 to 12 grains (0.58 to 0.77 Gm.) or more, or nembutal in sufficient quantities to insure the patient sleeping through the taking of blood pressures, is considered of considerable importance. Suitable cases should show a marked drop in the resting blood pressure levels, and it has been the Reviewer's experience that the final postoperative blood pressure levels very closely approximate the resting figures.

Sodium nitrite given in one-half grain (003 Gm) doses, repeated every one-half hour for three hours should have an appreciable effect in lowering the blood pressure to a basal level

The cold test is performed by having the patient immerse the hand up to the wrist in ice water to which salt has been added to bring the temperature to four degrees centigrade. Several blood pressure readings are taken immediately before placing the hand in the ice water to determine the mean pressure. One hand is then immersed and the blood pressures taken every half minute for from two to ten minutes The hand should be kept in the water for one minute if possible, but some patients cannot bear it more than 30 seconds sponse of increase in blood pressure of not over ten points is considered normal, from 10 to 20 points slightly abnormal and anything above this a markedly abnormal reaction. In some cases the systolic blood pressure may rise as much as 50 points as a result of the immersion of the hand in cold water. It is felt that

this reactive rise in blood pressure indicates the relative importance of vaso-constriction as a factor in the individual case, and the higher the rise in the systolic pressure, the more favorable is it considered as an index of the suitability for operation

The intravenous pentothal sodium test may be considered as the reverse of the cold test. It is felt that where nerve impulses play an important part in the production of elevated blood pressures, abolition of these impulses by an intravenous anesthetic such as pentothal sodium should result in a marked fall in the blood pressure levels. It would appear, therefore, that a case that demonstrates a marked fall would be a suitable one, whereas the case that falls very little, or none, should most certainly be unsuitable.

The test is simply performed, it being merely a matter of establishing the patient's blood pressure in a fixed position, preferably sitting or lying in bed, and then slowly administering the solution until the patient has completely lost consciousness. The blood pressure levels are determined at frequent intervals during this process until the patient regains consciousness, or until the blood pressure returns to the original level. It is felt that perhaps the blood pressure at the depth of complete unconsciousness is the basic level for that individual, and it could not be hoped that an operation would produce a lower sustained level

Allen and Adson state that incomplete studies indicate that pressure on the carotid sinuses may affect blood pressure to much the same degree that rest, amytal, sodium nitrite and pentothal affect it

The age of the patient undoubtedly is of great importance, and, in general, the younger the patient, the better the possi-

bilities. Some institutions established 40 as a maximum age earlier in their work, but now they have raised it to approximately 50 Crile⁶ does not feel that age is important, or rather, that age does not necessarily contraindicate operation since he feels that the degree of arteriosclerosis is much more important than the age of the individual Most authorities believe that 50 years is just about the maximum age, and that patients over that age offer very little chance of improvement

Any marked degree of arteriosclerosis is universally felt to be a definite contraindication to surgery

There seems to be no uniformity of opinion regarding the importance of duration of symptoms and rapidity of progress. In general, it may be stated that most authorities are of the opinion that cases in which hypertension has been present a relatively short time and has progressed rather rapidly, are less favorable than those of many years' standing with a relatively slow rise of pressure levels. Those of very short duration with a very rapid rise in blood pressure level usually are in the very malignant stage when first seen and are, therefore, unsuitable

The presence or absence and the degree of changes in the retinal arteries and optic discs are considered very important. Early retinal changes and minor degrees of spasm of retinal vessels can be determined only by skilled ophthal-mologists versed in this particular field. Retinal changes severe enough to be noted by the occasional observer, or frank choking of the optic discs, or retinal hemorrhage, are all evidences of malignancy, and indicate that the chance of surgery being of value is rather remote

The REVIEWER believes that the entire future of this field of surgery is dependent upon the proper selection of

cases. It is absolutely necessary that definite criteria of selection be established by means of which we may accurately select cases and foretell the approximate results.

The major purpose of the visits to the various clinics was to determine whether or not such criteria had been or could be established It is unfortunate. indeed, that one must report that at the present time this cannot be done There are two broad methods of error First of all, even though all of the tests may indicate that a case is highly suitable for surgery, yet the best we can hope for is just a little better than a 50 per cent chance of a good result On the other hand, occasionally a case that would seem to be absolutely hopeless from the standpoint of these tests when operated turns out to have an excellent result Therefore, it becomes impossible to accurately determine either one way or the other whether a case is suitable or unsuitable. or what our final result will be

This much may be said, however. The chance of a good result in a case that responds poorly to all or most of the tests is minimal. Operations in this type of case should rarely be undertaken. If we could be as accurate in determining which cases should be done as in determining which should not be done, our percentage of good results would be greatly increased.

The RIVILWER has made certain observations and has come to certain conclusions regarding the selectivity of cases for operation which he feels are worth noting. It has been our experience in a limited number of cases, just as it has been the experience of all others engaged in this line of work, that the "batting average" in any one test as compared with the final result does not get much better than 50 per cent. We feel, however, that the determination of

resting blood pressure levels offers a very accurate index. The patient whose blood pressure level does not fall at night when determinations are made without disturbing the patient, in our estimation offers a very poor subject for a good result following surgery regardless of what the result may have been of any of the other tests. We feel that this affords an accurate index of the effect of nervous and vasomotor impulses on the blood pressure.

The cold test may produce a marked rise, but does not indicate what may be expected in regard to a fall in blood pressure

The intravenous pentothal test introduces a profound chemical reaction, the effect of which upon the central nervous system may be such as cannot be approximated by surgery

It has been our observation that those cases that did not show a fall in resting blood pressure levels have shown no appreciable fall postoperatively and we, therefore, hesitate very much to advise operation in cases of this type regardless of what the other tests may show

Surgical Technic - Supradiaphragmatic Approach—This is practiced by various Continental surgeons and exemplified in this country by Peet 4 Peet resects the eleventh rib on each side Incisions are made parallel to the spinal column about three fingers' breadth laterally, centering on the eleventh rib section of rib about three inches long is removed and an extrapleural approach made to the splanchnic nerves and He removes apsympathetic trunk proximately four inches of the major splanchnic nerve from the level of about the ninth or tenth segment down to the point where it enters the diaphragm He then resects the entire sympathetic chain and ganglia from approximately the same

level to well into the diaphragm below The minor splanchnic nerve arising from the lower two or three thoracic ganglia may be a separate entity and is also removed well into the diaphragm. He insists that a careful dissection of the twelfth thoracic ganglion is necessary to be sure that the least splanchnic nerve is severed. This procedure is followed on both sides at the same sitting.

The question of whether this is the proper or a superior approach depends upon the determination of whether or not fibers from the first and second lumbar sympathetic ganglia play any part in the production of elevated pressures. Peet states that they do not. The Mayo Clinic group^{1, 2} feel that they play an important part in the innervation of the blood vessels of the kidney and it is, therefore, necessary that they be removed.

As far as the nerve supply to the celiac ganglion and plexus is concerned, Pect's operation is entirely preganglionic and if the same thing is true in this instance as has apparently been proved to be the case in Raynaud's disease this approach theoretically should be the most It has a further advantage tavorable in that both sides can be done at one operation. Its theoretical disadvantages are the mability to denervate the first and second lumbar ganglia and the fact that the fibers of the aortic plexus coming through the diaphragm with the aorta, which may play a considerable part in the production of vasospastic phenomena, are not interrupted. It has the further disadvantage that the adrenal glands may not be explored and the occasional case of tumor of the adrenal gland which may be causing the hypertension be overlooked

The question of whether or not a preganglionic operation is superior to a postganglionic operation in the case of hypertension has not yet been deter-

mined. The final determination must come after a period of years and a careful comparison of results.

Adson-Craig Type of Operation1-The technic of this operation has been described frequently. It consists of a subdiaphragmatic approach with or without the removal of a portion of the twelfth rib, the removal of the major. minor and least splanchnic nerves and a portion of the celiac ganglion. addition to this the first and second lumbar ganglia are removed and the dissection carried up into the diaphragm from below Recently, they have at times been removing the entire celiac ganglion Previously, a portion of the adrenal gland was removed, but they have abandoned this procedure being content to explore the adrenal glands determining the presence or absence of a tumor.

The disadvantages of this operation are that it must be done at two stages and that it is a considerably more difficult surgical procedure than that of Peet's This operation is somewhat of a hybrid, part of it being pre- and part of it being postganglionic. If the entire celiac gangha is removed, it becomes a truly postganglionic operation and as before stated this offers a theoretic disadvantage is apparently definitely safer than the Peet operation, a large number of these cases having been done at the Mayo Clinic without any deaths, whereas in Peet's series there has been a mortality of approximately four per cent

(nle Operation — This may be considered a modification of the Adson-Craig operation \(\) small incision just large enough to admit the hand is made in the flank just below the twelfth rib, carried forward and downward into the retroperitoneal space. He identifies the celiac ganglion by sense of touch, places a hook on it and removes the ganglion by cutting against his finger with a long

scissors and at no time visualizes the structures involved. In addition to this he states that he denervates the adrenal gland with his finger. The lumbar sympathetics are not disturbed and the various structures are not individually identified.

The advantages of this operation are the rapidity with which it may be done Its disadvantage is that it may very readily be incomplete as far as denervation of the celiac plexus is concerned In Crile's hands it is apparently an excellent operation. It is doubtful, however, that other surgeons could perform it with equal success. He has done a large series of cases, approaching 100, without a death, although previous to that series he had several deaths

The Intradural Section of the Anterior Root Components of the Splanchinc Verses (Heuer) —This operation requires a section of all the anterior roots from the fifth dorsal to the second lumbar, thus requiring a very long laminectomy and while the results in some of these cases have been excellent, the magnitude of the surgical procedure offers its greatest disadvantage

The Reviewer has performed a modification of the Adson-Craig operation starting with his first case, namely, the removal of the entire celiac ganglion and recently a section of the aortic plexus medial to the ganglion. This is entirely a postganglionic operation and the Reviewer teels that it accomplishes complete denervation of all vasomotor fibers on the postganglionic side. In all other aspects the operation is exactly the same as the Adson-Craig operation, the 11b being rarely removed. There have been no deaths in 15 cases.

Results of Surgery—It is quite amazing that regardless of the type of operation performed, all of the groups report

approximately the same results, namely, about 50 per cent good results and 50 per cent poor. Among those classed as poor, there are approximately half who received clinical and symptomatic improvement even though their blood pressures are not affected.

The Mayo Clinic reports 25 per cent excellent results, 30 per cent good results and 45 per cent poor results. Of the 45 per cent poor results approximately one-half show symptomatic improvement

Peet's results are very similar to those of the Mayo Clinic. The two institutions have about the same number of cases and the results measured from all standpoints are almost exactly parallel. The exact figures are to appear shortly in the literature.

Crile's results are rather difficult to evaluate since he uses as his criterion of result the decrease in diastolic pressure and disregards the systolic pressure, while other clinics use the drop in systolic pressure as their basis. He gives the following results

In all cases in which a follow-up was obtainable 32.2 per cent obtained drops in the diastolic pressure of over ten points. One to three months postoperative, 40.5 per cent good results, four to six months postoperatively, 331; per cent good results, seven to ten months postoperatively 35.3 good results. Fifty per cent of his cases over 50 years of age had drops of ten points or more in the diastolic pressure. Ninety per cent of the patients 35 years old and under had drops of ten points or more in the diastolic pressure. These figures were obtained from Dr. Cule personally

In a recent report from the Lakeside Hospital a series of 12 cases were reported in which Heuer's operation had been done, most of them with poor results

The Reviewer's results have shown approximately 35 per cent excellent results and another 35 per cent good results. In only three out of 15 cases has the result been such that it was felt that the operation was of no benefit. In all three of these cases the hypertension was of the very malignant type and operation was performed as a last resort with very little expectation of a success.

Comment-A number of years must elapse before this type of surgery in the treatment of hypertension can be either justified or should be abandoned The results up to the present time certainly warrant the continuation of this work From the results reported it may be assumed that we can expect an excellent result in at least 25 per cent of cases and a worthwhile result in another 25 per cent. This offers so much more than any other form of therapy that there seems to be no question whatsoever but that the work should be continued. Perhaps after another five years have elapsed it will have been shown that the operation is of value in only a few cases. On the other hand, it is extremely probable that much more accurate methods of selecting cases will be developed and if this is the case, the percentage of successful results will become infinitely higher. It is certainly most probable that this method of attack in the problem of essential and malignant hypertension offers a basis for the hope that the problem may some day be solved

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ENDOSCOPY

By Louis H Clerk, WD

BRONCHOSCOPY

Bronchoscopy for Foreign Body

The frequency of foreign body accidents, the hazards incident to the lodgment of foreign body in the larynx and the importance of foreign body in the bronchus as a cause of pulmonary suppuration, particularly bronchiectasis, have contributed greatly towards making the laity as well as the physician "foreign body minded". This is apparent in the diminishing number of reported cases of

foreign body of long sojourn Bronchoscopic removal still is the only method of treatment worthy of consideration. Foreign bodies, as common pins, in the periphery of the lungs, now can be removed by costophrenic bronchoscopy under fluoroscopic guidance thus rendering unnecessary a hazardous and mutilating transpleural approach. Bronchoscopists are agreed that bronchoscopic aspiration of secretion after removal of foreign body should be performed to prevent the development of pulmonary complications, notably bronchiectasis. In a follow-up study of patients discharged, presumably well, after foreign body removal, a number with bronchiectasis have been discovered. It is believed this could have been prevented if bronchoscopic aspiration of secretion had been performed following removal of the foreign body.

Bronchoscopy for Diagnosis

Improvements in technical equipment, the use of local anesthesia with appropriate sedation, the training of a large number of physicians qualified to perform peroral endoscopy and a more general employment of these procedures in diagnosis and treatment have aided immeasurably in allaying anxiety and apprehension concerning bronchoscopic procedures

Anesthesia—The toxicity of cocaine renders this anesthetic dangerous in children Larocain, in two per cent solution, is less toxic and may be employed with relative safety. In adolescents and adults instillation of from five to ten cubic centimeters of a two to five per cent larocain solution into the larynx and trachea by mirror laryngoscopy preliminary to bronchoscopy lessens laryngeal spasm and cough. As a result, endoscopic procedures may be carried out more effectively, the duration of the examination is shortened and discomfort to the patient is negligible.

Indications for Bronchoscopy— Among the obscure symptoms that often cannot be explained by the ordinary diagnostic procedures are wheezing respiration, cough and hemoptysis

Il heezing respiration is a symptom of partial obstruction of the trachea or bronchus. Obstructions may be endobronchial in origin without exhibiting any evidences of pulmonary or mediastinal disease. In these, bronchoscopy is clearly indicated.

Cough, resulting from bronchial irritation, may be induced by foreign body, benign or malignant endobronchial neoplasm, ulceration of bronchial mucosa or other bronchial lesions unassociated with demonstrable pulmonary disease Bronchoscopic examination is now considered as one of the important diagnostic aids

Hemoptysis of unknown origin, in the presence of negative chest findings no longer can be considered a contraindication to bronchoscopy On the contrary, direct inspection of the trachea or bronchi often may give a clue to the source of bleeding and may aid in establishing a diagnosis Among the common causes of hemoptysis in the presence of negative chest findings are ulceration, often tuberculous, of the trachea or bronchi, neoplasm and so-called dry bronchiectasis In three cases of recurrent hemoptysis of unknown origin reported by Gerlings,1 bronchoscopy revealed varices of the tracheal wall Early neoplasm, benign or malignant, must be considered These lesions can be diagnosed positively only by bronchoscopy How soon after hemoptysis should diagnostic bronchoscopy be performed? It is believed that this procedure may be dangerous if performed immediately after a copious hemorrhage In the presence of slight bleeding, however, it is considered important to proceed with bronchoscopy within one or two days after the hemorrhage then may trace the blood tinged secre-The danger of tions to their source provoking additional bleeding is slight if appropriate sedation and anesthesia are employed Controlling of pulmonary hemorrhage cannot be accomplished satisfactorily by bronchoscopy although packing of the bronchus has been resorted to

Neoplasm of Trachea and Bronchi

Papilloma of the trachea are of rare occurrence. In a study of the records of

314 cases of papilloma involving the upper airway, Lukens² found that in two the growths were primarily tracheal in origin. Dyspnea was a prominent symptom, voice disturbances were lacking. The diagnosis was made by bronchoscopy. Treatment consisted in reaming off the papilloma with the tip of the bronchoscope and removing them with an aspirating tube.

Carcinoma of the Bronchus

Collected data concerning cases of carcinoma of the bronchus show conclusively that the diagnosis commonly is made late in the disease when surgical treatment no longer is feasible. Clerf3 expressed the opinion that in a large number of cases, the diagnosis could have been made early if there had been an opportunity to carry out all of the recognized diagnostic procedures, notably bronchoscopy Bronchoscopic studies indicate that in a large number of the cases of primary caremoma, the growth occurred in a large bronchus Data concerning the anatomical location of primary bronchial caremonia vary greatly observers reporting from 35 to 75 per cent of growths as having their origin in the larger bronchi. The number of cases of caremona diagnosed positively by bronchoscopy and biopsy also varies obviously, this depends upon the type of case selected for bronchoscopic study. It performed only in cases of atelectasis or in advanced caremoma, the number of positive diagnoses would be nearly 100 per cent. The upper lobe is a common site. Bronchoscopic visualization in this group is difficult

Final diagnosis must rest on bronchoscopic biopsy if the growth can be visualized. In cases where it has not intruded into a large bronchus, the presence of fixity and rigidity of the bronchial wall may be accepted as corroborative evi-

The employment of 10d1zed oil dence to visualize the bronchi is valuable in cases where no conclusive information can be secured by bronchoscopy. The clinician should consider bronchial carcinoma as a diagnostic possibility and should carefully interpret the early symptoms, such as cough without or with sputum, blood-streaking, pain and wheeze The symptoms of advanced disease should not be waited for Radiographic studies should be secured early roentgenologist should be conversant with the clinical history and the symptoms Examination of the chest should include a study for obstructive emphysema

The bronchoscopist should be given an opportunity to investigate endoscopically all cases of obstructive emphysema or obstructive atelectasis. Bronchoscopic study should be considered when the early symptoms of carcinoma, namely cough, with or without sputum, bloodstreaking, chest pain, or wheezing respiration cannot be explained.

Bronchoscopic removal of caremona of the bronchus is practicable only in the rare case of well circumscribed or pedunculated growth. The excellent results secured by lobectomy or pneumonectomy and the mability of the bronchoscopist to ascertain the extent of infiltration of the bronchial wall or of extrabronchial involvement in a given case should suggest that surgical extripation is the method of choice. Bronchoscopy is of value in the advanced case for the placement of radium element into the involved bronchus.

Endobronchial intrusion of metastatic lesions from malignant growths elsewhere is not commonly observed. The common bronchoscopic observation in these cases consists of bronchial stenosis the result of compression. In these, biopsy is

hazardous since it necessitates biting through a normal bronchial wall.

Fungous Infection

Bronchomycoses, particularly aspergillosis, torulosis, moniliasis, sporotrichosis, blastomycosis, actinomycosis and coccidiosis, are of interest to bronchoscopists Looper4 discussed these various forms of fungous infection from a diagnostic and therapeutic standpoint, with particular reference to the bronchoscopic aspects Since these diseases can be diagnosed accurately only by bacteriologic examination, it is evident that bronchoscopy should play an important part in securing adequate materials from the lower air passages to aid in these studies In many the condition is diagnosed as tuberculosis, and, as a result, the patient may be retained in a sanatorium for long periods without securing appropriate treatment. Not only is bronchoscopy valuable in diagnosis but it occupies an important place in treatment. It has been shown that aspiration and local medication, similar to the methods employed in treating suppurative pulmonary infections, help in many of these patients

In considering the causal relationship of fungi to diseases of the respiratory tract Whalen? emphasized the importance of bronchoscopy in the diagnosis of pulmonary suppuration from undetermined causes. Granulation tissue from the brouch and secretions uncontaminated by bacteria from the mouth may be secured from the smaller bronchial subdivisions for study for fungi. No characteristic endoscopic picture has been observed in pulmonary suppuration due to infection with fungi, the appearances are identical with those observed in pulmonary suppuration due to pyogenic Securing tissue and secreorganisms

tion from the bronchi will aid, however, in the final classification of the disease.

Bronchoscopy in Tuberculosis

Important recent contributions have been made by bronchoscopic investigations in the field of tuberculosis Phthisiologists and thoracic surgeons have recognized the importance of bronchial obstruction which often is responsible for unexplained signs and symptoms as well as occasional unsatisfactory end results following surgical treatment discussing the three types of bronchial obstruction resulting from tuberculosis, namely, intramural, mural and extramural, Phelps⁶ emphasized the importance of bronchoscopy which has taught that tuberculous stenosis is not uncommon in chronic pulmonary phthisis. In children, a peribronchial gland may rupture into a bronchus, and then bronchoscopy may be a life-saving procedure In adults, bronchoscopy enables one to remove a broncholith, to diagnose ulceration or scar formation and treat them The bronchoscopist can aid the thoracic surgeon to decide on the type of operation he will perform, depending on the presence or absence of bronchial stenosis When operation does not give the patient complete relief, the bronchoscopist can frequently make him more com-Nonspecific bronchiectasis of fortable the lower lobe is a frequent complication of pulmonary tuberculosis in the upper lobe and develops as a result of tuberculous bronchial obstruction. Since information revealed by bronchoscopy is of such importance and the results of bronchoscopic treatment are so encouraging, one can safely say "No good sanatorum for tuberculosis is completely staffed without a bronchoscopist"

Although the opinion previously had been expressed that bronchoscopy was not indicated in the uncomplicated case

of tuberculosis, the recognition of tuberculous tracheobronchitis as a clinical entity now demands that direct examination be employed to make a final diagnosis. Repeated endoscopic examinations are valuable not only to ascertain the presence of a lesion, but also to determine if it is progressive or regressive Samson7 considers these observations of value in determining what type of collapse therapy, if any, should be employed Bronchoscopists experienced in the study of tuberculous patients are agreed that the combination of several of the following signs and symptoms in any patient should be considered as of sufficient importance to warrant bronchoscopy, namely constant wheezing, either expiratory or inspiratory or both, after all sputum has been raised, extremely thick, tenacious sputum difficult to raise; marked variation in quantity of sputum from day to day, abnormally large amounts of sputum trequent or persistent presence of organisms in the sputum in spite of apparent control of the parenchymal lesions, unexplained elevations of temperature and intermittent areas of atelectasis, as seen in serial roentgenograms of the chest

There is a difference of opinion relative to bronchoscopic biopsy of bronchial lesions in suspected cases of tuberculosis The opinion is expressed that biopsy may lead to miliary or parenchymal spread from uncovering new avenues of dissemination in the tracheal or bionchial lesions. This must depend upon the findings in the individual case known case of tuberculous ulceration biopsy is unnecessary. In undiagnosed ulceration, the question of carcinoma also must be considered Here a positive diagnosis is imperative and biopsy must be resorted to

The accessibility of tuberculous lesions of the trachea and bronchi to broncho-

scopic visualization has led to endoscopic measures in treatment Strictures resulting from healed ulcers have been dilated Kernan⁸ summed up the bronchoscopic aids in the treatment of tuberculosis of the trachea and larger bronchi as follows Ulcers may be treated by coagulation with diathermy, topical applications of silver nitrate or the quartz rod, strictures are stretched with copper ionization, tuberculous tumors may be removed with forceps or coagulated with diathermy, obstruction produced either by a mass of thick secretion or caseous material from a cavity or ruptured lymph nodes may be relieved by bronchoscopic aspiration, secondary abscesses or bronchiectasis occurring beyond strictures may be relieved by aspiration

Asthma

The best results from bronchoscopic treatment in asthma are secured in cases of tracheobronchitis with excessive secretions which tend to produce partial bronchial obstruction. Bronchoscopy should also be tried in cases in which there is no demonstrable etiologic basis for the symptoms or in which the condition does not respond to treatment based on supposed causative factors. Vaccine made from bronchoscopically removed secretions has been found valuable in instances of so-called bacterial allergy.

Pulmonary Abscess

The fundamental principles underlying the treatment of abscess of the lung remain unchanged. Whether drainage can be established and maintained adequately by conservative measures without or with bronchoscopy or by external surgical drainage must be determined in the individual case. In cases complicated by bronchial obstruction diagnostic bronchoscopy is indicated to rule out foreign body, neoplasm or other lesion. The best

results are secured if bronchoscopy combined with medical treatment is instituted early in the disease

In a review of the literature of pulmonary abscess. Mathews9 found that there was an increasing frequency of occurrence in children He expressed the opinion that the wholesale removal of tonsils in children may account for this increase In support of the aspiration theory of infection is the observation that the right lung was involved more often than the left It is of interest to note that fusiform bacilli and spirochetes common in cases of abscess in adults were not found in children Medical treatment for a period of six weeks was recommended If there was no improvement, bronchoscopic aspiration was recommended, if progress became stationary, surgical treatment was advised The prognosis is favorable particularly when compared with the results in adults

In bronchoscopotherapy, the procedures discussed by Soulas10 consist of aspiration of secretions, topical applications, cauterization, catheterization of bronchial orifices, removal of granulations instillation of solutions in small quantities and lavage of the main bronchi It is important to recall that one cannot penetrate the lung with the bronchoscope in order to carry out treatment results in obstructive lesions often are simple and rapid owing to removal of a cause which is mechanical This was observed in a woman who vomited and aspirated material after an operation under general anesthesia. Asphyxiation was prevented by prompt bronchoscopic removal of the aspirated material

In certain cases of bronchopneumonia, signs of asphy viation due to large quantities of mucopurulent secretion are observed. The author successfully treated three such cases bronchoscopically

Bronchiectasis

The earlier reports of bronchoscopic treatment gave the impression that bronchiectasis could be cured by this means. With a more general employment of iodized oil for lung mapping it has been shown that dilated bronchi in bronchiectasis rarely are restored to normal although the infection may clear up and the patient become symptom-free. Bronchoscopy, however, has a definite place in the prevention, diagnosis and treatment of bronchiectasis.

Bronchial obstruction undoubtedly is one of the most important factors in the etiology of bronchiectasis Obstruction interferes with drainage of bronchial secretions The retained secretions become infected, there is inflammation of the bronchial mucosa with increased production of bronchial secretion, interference with lung function and ultimately sufficient structural changes in the bronchial walls to lead to bronchiectasis If recognized promptly, the obstruction may be removed or relieved bronchoscopically, thus re-establishing drainage of the bronchus, ventilation of the involved lung and clearing up of infection. If there has been little damage to the bronchial wall, restoration of function may be complete and in this way bronchiectasis can be prevented

In the obstructive forms of bronchiectasis, an etiologic diagnosis can be arrived at only by bronchoscopy. These cases often are benefited by removal of the obstruction to drainage and repeated bronchoscopic aspiration of pus. Notable examples of these are cases of foreign body, benign neoplasm and stricture. As an aid to the thoracic surgeon, preoperative bronchoscopic aspiration of pus will benefit the patient by decreasing the frequency of cough, reducing bronchial infection and diminishing sepsis. In bi-

lateral bronchiectasis and in those with unilateral disease not suitable for surgical extirpation, bronchoscopy may be given a trial, particularly if postural drainage is not effective

Pneumonography

The introduction of iodized oil into the bronchial tree as an aid to the roentgenologist has contributed immeasurably to our knowledge of pulmonary disease. Many methods of introduction of the oil are employed. The important criteria are placement of the iodized oil in the bronchus to be visualized and its retention until roentgenoscopic or roentgenographic observations are made. While the bronchoscopic method has been replaced, in part, by various in-

direct methods of instillation it is the only practical method in cases of bronchial obstruction

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ESOPHAGOSCOPY

By Louis H (LIRI, MD

Congenital Deformities

Among congenital deformities of the csophagus the most common is congenital atresia, either complicated or not with tracheo esophageal fistula. From a clinical standpoint however the most interesting cases are congenital stenosis of the esophagus. In discussing the form of congenital stenosis usually referred to as congenital short csophagus," Gerlings1 reviewed the reported cases and concluded that it appears to be a comparatively frequent deformity. The esophagoscopic findings usually characteristic, consisted of dilatation of the upper portion of the esophagus with chronic esophagitis, a stenosis of the lower thoracic esophagus which is "funnel-like" or "web-like," generally with ulceration which is superficial and covered with thin gray exudate, gastric mucosa immediately below the stenosis and in some cases a peptic ulcer of the esophagus

Although this form of deformity is considered by some writers as a separate group of hiatus herma. Gerlings agrees with other observers that if one considers the genesis of herma, there is no question of any real herma in these. For a roentgen diagnosis two factors must be observed. Examination of the patient in the right-oblique-prone position which brings the hiatus esophagus at a higher level than the remainder of the esophagus, and, filling of that portion of the stomach below the diaphragm

The narrowing at the esophago-gastric junction differs little from organic stenosis. Certain of the reported cases were originally considered as cicatricial stenosis and the true nature was not discovered until the stenosis was traversed by

esophagoscopy The prognosis usually 15 good. Treatment consists of dilatation of the stenosis.

Benign Neoplasms

Benian neoplasms of the esophagus are considered as of rare occurrence. The relatively mild symptoms of esophageal obstruction and reticence on the part of internists to have esophagoscopy performed for diagnosis may be responsible, in part, for this apparent rarity. In Hunt's2 case, daily gastric lavage had been carried out by the patient herself for a period of 30 years before an esophagoscopic examination was performed At this time malignancy was suspected but esophagoscopy revealed ulceration in the lower esophagus, varicosities and a moderately tight cardia. Five years later esophagoscopy revealed multiple growths below the cricopharyngeus and above the cardia The histologic diagnosis was papilloma

Carcinoma of Esophagus

In spite of a voluminous literature dealing with the diagnosis and treatment of carcinoma of the esophagus, the end results would indicate that remarkably little progress has been made sidious onset with relatively few symptoms until the growth has attained considerable size, usually results in late diagnosis this in spite of improved roentgenographic technic and esophagoscopic study. Little progress in treatment can be hoped for until every patient with any symptoms, however vague, referable to the esophagus is subjected to esophagoscopy Surgical treatment of carcinoma of the esophagus has been successful in a few cases. Irradiation and other forms of therapy have been practiced with little success Moersch[‡] reported the successful treatment of a case of early carcinoma of the esophagus by surgical diathermy The carcinoma, a polypoid tumor, originated from the right wall of the esophagus at about the level of the aortic arch Biopsy was reported as squamous cell carcinoma. grade 2 Because of the patient's age (68 years), the location of the growth and its polypoid character it was considered advisable to resort to destruction of the growth by surgical diathermy rather than surgical extirpation thermy was performed esophagoscopi-Several small areas of infiltration of the esophageal wall were subsequently destroyed by coagulation and two courses of roentgen therapy were administered The patient has been kept under observation and there have been no recurrences in over two years

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GASTROSCOPY

By Louis H Clerk, M D

The perfected flexible gastroscope provides a safe and simple means of observing the interior of the stomach and a useful aid to the methods of investigating gastric disorders. Disturbances in gastric motility, gastric retention and alterations in contour are observed by roentgen studies. Gastroscopy affords little or no information concerning gastric function Its value is dependent upon studying the

appearances of the interior of the stomach. Erosions, mucosal hemorrhage, changes in the color and appearances of the gastric folds as well as large ulcers and neoplasms can be readily visualized. This method produces less distress and permits examination of a larger portion of the interior of the stomach than does rigid tube gastroscopy. A majority of gastroscopists are agreed that esophagos-

the stomach were recorded None terminated fatally In a study to ascertain the cause of these accidents, Schindler and Renshaw¹ found that the sponge tip does not deflect the end of the gastroscope when the gastric wall is met with nor does it facilitate bending. As a result the pressure of the advancing end is localized to a small area beneath the sponge tip The rubber finger tip, which

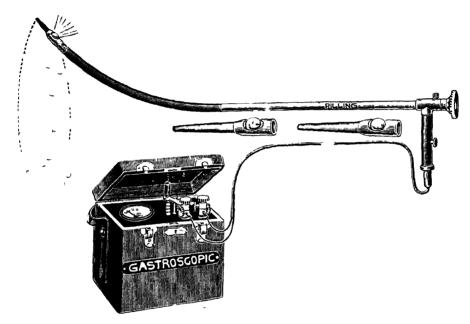


Fig. 1—This illuser tool shows the flexible gastroscope with cord and battery attached. The bulb used for inflation not shown in the illustration is attached directly opposite the battery cord attachment. The distal end is equipped with a flexible rubber finger. Immediately proximal to this is a powerful incandescent lamp. Two lamps and rubber fingers are shown independently. The flexibility of the distal portion of the gastroscope and the lateral placement of the objective have added greatly to the field that may be inspected at any one time as well as the visibility of practically every portion of the stomach.

copy as a preliminary to gastroscopy is unnecessary in the absence of symptoms or roentgen evidence of esophageal disease

An important technical improvement to the flexible gastroscope is the substitution of a flexible, rubber finger tip for the rounded sponge tip (Fig 1). The addition of the sponge tip to the gastroscope rendered the instrument unsafe. In 360 examinations carried out with the sponge-tipped tube, five perforations of

the line of least resistance and initiates bending of the flexible portion, thereby distributing the pressure more evenly. It is therefore essential for safe gastroscopy to use the flexible rubber finger tip. In several thousand examinations carried out with this no perforation has occurred

The relative simplicity and safety of flexible tube gastroscopy if a few simple precautions are observed and the large area of gastric mucosa that can be inspected renders it an invaluable aid to the gastroenterologist, roentgenologist and surgeon. It is indicated not only to confirm the roentgen diagnosis of ulcer or neoplasm but is especially valuable in the investigation of patients with gastrointestinal symptoms in the presence of a negative roentgen study. It is not offered as a subsitute for roentgen study; instead the result of medical treatment of chronic ulcer, in fact, it provides the most reliable criterion of the healing of an ulcer

A more enlightened viewpoint concerning the existence as well as the prevalence of chronic gastritis has resulted from gastroscopic examination of cases of so-called "gastric neurosis." Although chronic, nonspecific gastritis

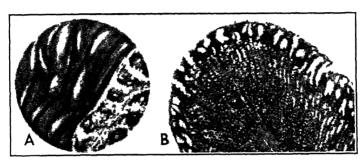


Fig 2—Superficial gastritis A, gastroscopic picture reveals thick purulent secretion B, microscopic section shows advanced cellular infiltration only of the upper layers of the mucosa (From Shindler, Ortmayer and Renshaw Jour A M A, Feb 6, 1937)



Fig. 3— Atro, the gastritis of gastroscopic picture suggests thinning of mucosa greenish aray and prominent submucosal vessels B, microscopic section shows thinning of mucosa, absence of glands and metaplasia Development of goblet cells (From Shindler, Ortmayer and Renshaw Lour A. M. A., Feb. 6, 1937.)

It is a valuable supplementary aid to the rochtgenologist in making an early diagnosis of carcinoma, in differentiating between a benign and a malignant lesion, in determining the extent and location of a lesion and in excluding intragastric pathologic involvement

One usually has little difficulty in recognizing benign ulcer and differentiating it from carcinoma. Direct inspection has been found valuable in checking

was not considered as a clinical entity for many years, recent gastroscopic studies using the flexible gastroscope have demonstrated conclusively that it is of common occurrence and must be considered as a major problem in internal medicine

In a study of the subject of gastritis, Schindler and others? made observations on 2500 patients examined gastroscopically, all of whom had abdominal com-

plaints. In 23 per cent, the gastroscopic appearances were normal. About 50 per cent of the cases presented changes indicating chronic inflammation of the gastric mucosa, namely, layers of whitish, gray-

did not change in later examinations. The mucosa appeared thin and greenish-gray and protruding blood vessels were seen. This condition was considered as "atrophic gastritis" (Fig. 3)

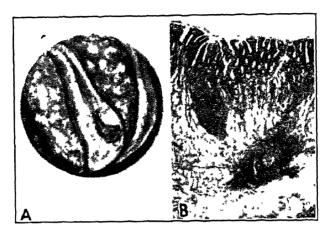


Fig. 4—Hypertrophic gastritis—4, gastroscopic picture reveals swelling and nodular appearance in the valleys erosion surrounded by hemorrhagic area on central fold—B, microscopic section shows enlarged lymph nodes with extensive interstitial infiltration throughout entire microst—Proliteration of the surface epithelium—(From Shindler, Ortmayer and Renshaw Jour V.M. V. Leb. 6, 1937.)

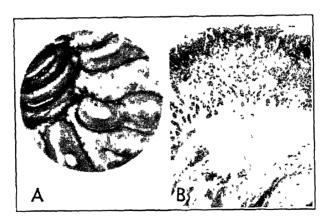


Fig. 5—(ristritis of postoperative stomach—1 gastroscopic picture reveals jejunum visualized (left upper quadrant) erosions on edematous gistric tolds purulent secretion between tolds B, incroscopic section shows thickening of submucosa with scattered areas of infiltration—Extensive infiltration of the mucosa with erosions partly covered with exudate—(From Shindler Ortmaver and Renshaw Jour A. M. A., Feb. 6, 1937.)

ish or greenish mucus or hyperenic spots. These changes were designated "superficial gastritis" (Fig. 2). Some cases in this group exhibited changes at subsequent gastroscopic examinations. Thin greenish-gray spots appeared that

A third form, a separate clinical entity, is "hypertrophic gastritis". In this, the mucous membrane appeared swollen, thickened, velvety and often containing hemorrhages and erosions and showing nodules or large nodes, creases and

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crevasses (Fig 4). No atrophy develops in this form.

Another form of chronic gastritis has been observed in the postoperative stomach. This exhibits all the three previously described forms of gastritis, superficial, atrophic and hypertrophic. This offers the worst prognosis (Fig. 5).

The authors surveyed 228 cases of gastritis and selected for analysis 53 that exhibited the most marked and typical gastroscopic picture unassociated with any other disease. The average duration of symptoms was five and a half Hypertrophic gastritis predommated in the male while the other forms were equally distributed The subjective symptoms varied In a study of the symptoms, they were unable to formulate a typical clinical picture In their experience physical examination, gastric analysis and roentgen study gave little aid in making the diagnosis Gastroscopy with the flexible tube afforded the only evidence upon which an accurate diagnosis could be based

The use of the flexible tube gastroscope offers a means of determining precisely the conditions which give rise to a recurrence of symptoms following operative procedures commonly performed for the relief of gastric or duodenal ulcer or the removal of carcinoma examined gastroscopically a group of 15 patients previously operated upon for gastric disorders who had a recurrence of symptoms. In all cases he found some condition to explain the complaints or abnormalities noted by x-ray examination He directed attention to the rather frequent occurrence of gastritis and that several types of gastritis often are seen in the same stomach Schindler had previously classified this as "gastritis of postoperative stomachs" Gastroscopy affords the only opportunity of visualizing directly such changes as may occur in gastric mucosa following a poorly functioning opening placed in the stomach as part of some operative procedure

Gastritis of various degrees more often is observed following gastroenterostomy done for duodenal ulcer than for any other type of operation. Gastroscopy is important in these cases not only to determine the presence of gastritis but also to ascertain the formation of new ulceration or malignancy

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CANCER

CLARK E BROWN, BS, MD

Etiology—A Fischer¹ sets about to answer the question of what cells in an apparently normal tissue subsequently go to make up a cancer. He calls attention to the fact that cell multiplication is common to both cancer and regenerating normal cells. He points out that normal cell regeneration and cancer are cellular.

multiplications resulting from cellular injury. Noting these similarities he asks whether cancer arises from a transition of normal cells or from cells with malignant properties which are already present in normal tissues. The distinction of these isolated malignant cells from their surrounding normal neighbors is

not possible histologically. The author believes that his experimental data are strongly suggestive of the thesis that malignant cells occur in histologically normal tissue. In order to give these cells adequate growth opportunity the method of repeated autologous transplantation The breast tissue of was employed voung mice, most but not all of which were pregnant or lactating, was transplanted into other portions of the body, usually the subcutaneous tissue of the flank After a lapse of a few weeks, the tissue was again transplanted to another portion of the same animal's body After one or more autologous transplants of this supposed normal tissue a mass formed at the transplant site which on section resembled carcinoma these in fact metastasized to the lung \ large number of experiments were necessary for a few takes, but the results are no less astounding. The author believes that these tumors resulted from offering the rare malignant cells, usually held in abeyance by the normal tissue resistance, an opportunity to grow. Thus the cells with the highest proliferative tendencies and adaptabilities for survival were allowed through natural selection to terminate in genuine malignant tumors To quote '--- the cancer cell is already present and needs only what may be termed a realization factor to develop into a malignant tumor" This theory appears somewhat similar in the REVIEWER'S opinion to that expressed by S. P. Reimann of Philadelphia and called by him the 'Spare Parts Theory"

In 1933 Yoshida reported the production of typical liver cell carcinoma in a group of rats fed o-amidoazotoluol for something over nine months. This chemical is the active constituent in the scarlet red molecule, a dye used previously to stimulate epithelial regeneration. Histologically these tumors resembled hep-

atomas The sequence of events in the development of the cancers was liver cell hyperplasia, then adenomas, then carcinomas which metastasized M Shear² confirms these findings. He injected a glycerol suspension of o-amidoazotoluol six times at bi-monthly intervals in doses of 10 mg each into 23 pure strain mice After a year over half the number developed liver cancer These were successfully transplanted subcutaneously into other mice In one series the transplant grew through ten generations. Histologically the transplants retained their liver cell nature One animal developed an adenocarcinoma of the large bowel Since the chemical is a pigment the author raises the question of the rôle of pigments in general in the genesis of cancer It is a noteworthy fact that while primary liver cancer is rare among white races it is fairly common in pigmented races

A study of the combined action of the carcinogenic 1-2-5-6 dibenzanthracene and the hormonal substance theelin has been reported by I H Perry and L L Ginzton ³ Half of a large group of 150 adolescent female mice was splayed Half of the splayed mice received 1-2-5-6 dibenzanthracene alone, and the remainder received dibenzanthracene and theelin The unsplayed mice were treated similarly. Both substances were applied to the skin Breast carcinomas developed in the groups as follows

Group I—Normal Mice with Dibenz (25)

—0 carcinoma

Group II—Normal Mice with Dibenz and Theelin (14)—6 carcinoma—43 per cent

Group III—Splayed Mice with Dibenz (37)
—4 carcinoma—11 per cent

Group IV—Splayed Mice with Dibenz and Theelin (15)—7 carcinoma—45 per cent

Seven breast tumors metastasized and four were multiple Cervical carcinomas

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were produced, two in mice with mammary cancer In the theelin mice hyperplasia of the uterus was noted Animals treated with dibenzanthracene only developed carcinoma of the skin, lung, breast, stomach and colon The authors state that these are the first carcinomas of the breast and alimentary tract produced by dibenzanthracene alone. The strain of mice employed was a nontumor bearing strain Myoblastomas, lymphoblastomas and thymomas were also produced In addition to these, benign tumors such as papillomas of the skin, uterus, vagina, lung, kidney, stomach, colon and bladder occurred. Sebaceous cysts, adenomas of the lung and nasal sinuses, cystadenomas of the meibomian glands and breast and cysts of ovaries also developed From this array the authors conclude that since many of these benign proliferations occurred before the development of the cancers they were probably casually related to the subsequent malignancies

Pathology—J Ungar, Jr, and S Warren4 entertain the question of whether cell injury from x-rays is due to direct effect on the cell itself or to a secondary environmental effect They attempted to answer this question by an ingenuous method A dose of 120 millicurie hours of beta and gamma rays was delivered by contact to rabbit's ears. The irradiation source was glass tubes of radon in a steel jacket 0.4 mm thick filtered only through a layer of rubber A piece of skin thus irradiated was transferred to the exposed corium of the opposite ear. In turn the normal skin was transferred to the corium of the irradiated ear. In no case did the non-irradiated skin grow on the irradiated corium, but in 32 per cent of the 55 grafts of irradiated skin to normal corium did subsequent takes ensue The authors theorize that in the irradiated epithelium the changes were sufficiently reversible to allow continued growth under proper nutrition. They conclude that the beta and gamma irradiation effects on the rabbit's skin must have resulted from both direct and indirect activity.

The diagnosis of malignancy from sediments of pleural and peritoneal effusions is frequently as difficult as it is important. The usual methods for preparation of these specimens for microscopic examination are but two, the smear and the paraffin section technics The various modifications of these two are protean N C Foot⁵ has reviewed the subject and has evaluated the various criteria for the determination of malignancy in an examination of these effusions He has not included a consideration of the cellular findings in sputa and gastric contents because of the unsatisfactory effects of these materials on cellular histology Although many pathologists employ fresh smears of the pleural and peritoneal effusions stained supravitally, the author has followed the method of fixed preparations similar to that devised by Mandelbaum The effusion fluid is centrifuged. If there is a large quantity, sufficient glacial acetic acid is added to bring the concentration up to two per cent. This prevents coagulation and lakes the excess erythrocytes The button formed in the bottom of the centrifuge tube is fixed in ten per cent formalin in 95 per cent alcohol The button is imbedded in paraffin on its side and stained by Masson's trichome light green method Other stains are applicable but the author prefers the above because the nucleoli are readily stained and measurable

The author reviewed his results in 55 specimens of ascitic fluid and 85 of pleural fluid collected over a $3\frac{1}{3}$ -year period. The accuracy of the diagnosis was checked by autopsy, biopsy, opera-

tion, x-ray and the clinical history. The average for correct diagnoses was 65 5 for abdominal fluid and 68 5 per cent for thoracic fluid When the series was limited to cases confirmed by autopsy, biopsy, or operation the abdominal fluid showed 69 per cent positive and the thoracic fluid 65 per cent In cases where no tumor was present the abdominal fluid showed 58 per cent correct and the thoracic 89 per cent

The chief source of diagnostic difficulty lay in the recognition of the mesothelial cell This cell is present in most types of effusion and presents many features by which cancer cells are identified such as occurrence in clusters. multinucleation and mitosis In differentiating between the two, advantage is taken of the ratio between nuclear and nucleolar diameters. In malignant cells the nucleolus is larger in proportion to the nucleus than in the normal cell To evaluate this criterion the author measured the above diameters in ten doubtful cells in each section. These were averaged If the n/N (n-nucleolus, N-nucleus) ratio showed 0.20 or under, no tumor was present, but if it was found to be 0.25 or over tumor was assumed to be present A few specimens showed ratios between the two figures Out of 44 sections so judged 68 per cent were proven correct. This encourages the utilization of this ratio for the diagnosis of malignancy in effusions. The author emphasizes the validity of A P Zemansky's6 criteria, namely the finding of cells arranged in acini or papillae overlying a fibrovascular stroma Multinucleation and the presence of mitoses per se were judged valueless, but monster or abnormal mitoses were accepted as indicative of tumor cells Erythrocytes or fibrin were of little diagnostic help

Therapy—Little is known of the finer details of cellular injury taking place

at varying periods after x-ray exposure P. J. Melnick and A Bachem⁷ have studied the problem with the idea of determining the type and time of appearance of degenerative phenomena in tumor cells following x-rays administered by four dosage technics in which the time factor is the variable. The tumors employed for study were the Flexner-Jobling rat carcinoma, the Jensen rat sarcoma and the Walker rat tumor 256. These tumors were transplanted into the subcutaneous tissue of the mid-back. The treatments all started the tenth day after inoculation, at a time when the transplants had reached the approximate size of a pea The tumors were measured daily for two weeks then twice weekly Six weeks after the beginning of the treatment all rats surviving were killed. All tumors were studied histologically The x-ray irradiation methods were as follows

- 1 Controls—no irradiation
- 2 A single massive treatment of 1 to 16 minute duration (185 to 2960 r)
- 3 Fractional daily treatments of ¼ to 1 minute duration (46¼ to 185 r for totals of from 350 to 5550 r)
- 4 A modified fractional technic whereby fractionated daily dosage was given as in No 3, but was split up further into 5 or 10 second fractions with two minute intervals. Thus each daily treatment was spread over a total of 6 to 12 minutes.
- 5 The saturation technic with initial dura tion of from 1 to 6 minutes delivering 185 to 1110 r, followed by daily administration for ½ to ½ minute

Measurements of these tumors and their histologic study after these various treatments have brought out several facts, many of which confirm previous experiments The Walker 256 proved to be too radioresistant to yield much data

Two types of degenerative changes were noted in the tumors in general One was the well recognized primary

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degenerative effect characterized by pyknosis of the nuclei and karyorrhexis This was assumed to have occurred in those tumor cells in mitosis, and characterized the immediate lethal effect. The other effect is a more remote one and developed later with the production of abnormal forms such as giant cells which eventually calcified These later changes are assumed to have occurred in tumor cells refractory to the immediate primary effects of the x-rays Through suffering chromasomal injury they survived to reproduce abnormal forms which ultimately calcified Thus we have presented the effect in tumors described by Muller in his work on Drosophila.

The authors found the effect of the small divided doses in producing the abnormal cellular forms cumulative The protraction of this divided dose technic as in No 4, was no more effective than No 3 One might have anticipated the opposite because of the greater chance of the spread in dosage catching a greater number of cells in mitosis But the authors point out that it is practically impossible to irradiate a large number of cells in mitotic division unless irradiation is constant. The most effective type of dosage distribution used to eradicate the tumors was the saturation By this method a primary degenerative effect is produced in the sensitive cells in mitosis, and the subsequent divided applications destroy the refractory cells by inducing them to produce abnormal forms which fail to sur-

G T Pack and L R Taber⁸ describe a radium element seed costing about \$60 each for use in tumor therapy in the absence of facilities for making radon seeds. The seed is a tiny cylinder measuring 7.5 mm by 1.2 mm. externally. The filtration employed is 0.3 mm of platinum. The radium content of each

unit is 133 mg In a little over four days the authors state that each seed delivers a dose of one millicurie destroyed. The seeds are inserted through trocar needles having a diameter of 1.8 mm. Attached threads make their withdrawal after operation possible Their maximum utility in interstitial radiation is in situations where radium needles are too large or cumbersome. The authors have used them mostly about the mouth, in which case the patient is fed a liquid diet through a nasal catheter. Other sites such as the face, bodily skin and lymph nodes offer good fields for their application

Brain Tumors — The treatment of brain tumors always offers interesting problems Their surgical treatment is a comparatively recent development and their reaction to x-rays is still a point for elucidation C. H. Frazier, B J Alpers, E. P Pendergrass and G W Chamberlin9 have attempted to determine the effective irradiation dosage in the treatment of gliomas The actual curative value of this method of treatment in gliomas is questionable Whether x-rays will prolong life as an adjunct to surgery or where surgery is impossible is another matter. But from the standpoint of cure it is essential to know what dosage is necessary to kill all cells in a given glioma. With this end in view the authors studied 30 cases of glioma in which histological specimens were available before and after irradia-These offered rare occasion for an interpretation of irradiation effects Comprising the tumors were 12 medulloblastomas, seven glioblastomas multiforme, six astrocytomas, two ependymomas and three oligodendrogliomas

Study of the most radiosensitive of the group — the medulloblastomas, after an apparently adequate course of irradiation, showed only about one-fifth the tumor

cells affected by irradiation. Among the seven glioblastomas only four showed histological changes ascribable at all to irradiation, warranting the conclusion that this tumor is only slightly radiosensitive Contrary to expectation half the cases of astrocytoma showed histological changes from irradiation In two of the tumors there was an apparent maturation tendency Thus some astrocytomas are radiosensitive Both ependymomas showed irradiation effects, but none of the oligodendrogliomas showed microscopic changes The authors as a result of these findings emphasize that if radiologic cure is sought, heavy irradiation through many portals at frequent intervals is necessary. It is inferred that much of the irradiation treatment to date has been insufficient both as regards series frequency and total dosage

\nother raier type of brain tumor in which rather surprising therapeutic results occurred are the hypophyseal stalk tumors R C Carpenter, G W Chamberlin and C H Frazier¹⁰ report a series of 12 cases. In eight the treatment was only surgical. Only one of this group was alive and fairly comfortable 30 months after operation. In a group of four cases treated by aspiration and deep x-ray therapy, all were alive and well 301, months after treatment Considering the fact that these cystic tumors are lined with histologically mature epithelium the effect of irradiation was assumed only to have delayed refilling of the cysts through inhibition of secretion Radical removal of these cystic tumors carries a high mortality because of the implication of the wall of the third ventricle

Intra-oral and Peroral Carcinoma
—Irradiation of intra-oral or peroral carcinoma has presented the constant difficulty of reactions in interposed normal tissues Osteomyelitis of the mandibles

or radionecrosis of the soft parts offers serious obstacles to the full dosage of external irradiation for intra-oral cancer H E Martin¹¹ has perfected and systematized a method for x-ray irradiation of the tongue, buccal floor, jaws. cheeks, tonsils, palate, maxillary antra and posterior nasopharynx through the open mouth as a portal of entry. Direct application of the rays to the lesion has been possible by the use of lead-lined brass tubes varying in diameter from 25 to 4 cm These are interchangeable on the machine and are selected according to the size of the lesion. They serve as retractors for the soft parts and insure delivery of the dosage to the tumor alone. The author has used the follow-200 KV, 6 ma 35 cm ing technic skin target distance and 05 mm of copper as filtration The dosage is fractionated between 200 and 250 r for 20 daily doses in treating a 25 cm lesion through a 3 cm cylinder Larger individual doses given over a two week period may be used For delivery through a 4 cm portal, 150 to 200 r daily are given for a total of 3000 to 4000 r Such a régime, although it may cause complete disappearance of the lesion, is followed immediately by implantation of radon seeds The author states that consistent failure to employ the secondary interstitial irradiation will lead to a certain number of recurrences Such a technic places intra-oral cancer in the category of many skin cancers. The curability of these lesions is on the increase because of the increased accessibility

Carcinoma of the Pancreas — The absolute hopelessness of the situation in the great majority of carcinomas of the pancreas is a matter of common knowledge. An appreciation of this fact led J. D. Rives, S. A. Romano and F. M. Sandifer 12 to inquire carefully into a series of cases to uncover if possible

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some diagnostic aides for early diagnosis Their study included 96 cases of carcinoma of the pancreas verified by operation or autopsy The histories of these patients were studied in detail to ascertain any symptom complex or laboratory tests which might point to an The results, although early diagnosis disappointing in the light of this quest, brought to light the following facts The disease is four times as frequent in men as in women About three-fourths the cases occur in the head of the pancreas The liver is the most common metastatic site with the regional nodes, omentum and mesentery next in the order of frequency Seventy per cent of the 41 autopsied cases showed liver metastases The x-ray was of the greatest diagnostic value of any single laboratory test. The chemical studies on the stool were disappointing Signs of extrinsic pressure on the duodenum with widening of the duodenal loop were considered significant from the roentgenologic standpoint The most frequent maugural symptoms of the disease were pain, then jaundice Radical operation was referred to as the only hope of saving these patients from a rather prompt death. None such successful cases were presented in the authors' material In their autopsied cases the authors judged that there were eight patients whom radical operation might have saved

Carcinoma of the Breast—Through the work of Loeb, Cori and Murray it has been known for some time that castration diminished the incidence of mammary cancer in mice W E Herrell¹³ has made the following observations with relation to human breast cancer. He reviewed 1906 records of women treated for cancer of the breast and 1011 records in a similar age group without mammary cancer. He noted the incidence in each series of cases having a

previous complete oophorectomy. In the cancer group the incidence of oophorectomy was 15 per cent before the diagnosis of breast cancer, and in the non-cancer group the castration incidence was 15.4 per cent Such a finding appears significant

Leiomyoma of the Uterus-It is interesting from time to time to reconsider the question of irradiation versus surgery in the treatment of leiomyoma of the uterus C F. Burnam14 discusses the value of external irradiation in treating patients over 40 years of age in whom the diagnosis is certain and in whom there is no complicating pathology In this type of patient the surgical mortality varies between one and five per cent The author presents 1800 cases of uterme fibroids treated with irradiation with no deaths In 100 consecutive cases with uterine hemorrhage from leiomyomata treated with external or combined external and internal irradiation, 59 tumors completely disappeared All but nine showed some reduction, and none of the latter required hysterectomy. In his discussion of this paper Dr W P Healy emphasized the importance of diagnostic curettage to eliminate a malignant tumor preliminary to any uterine radiotherapy

Teratomas of the Testicle - The question of whether preoperative irradiation in general increases the chances of subsequent operative cure deserves a place in any discussion of malignancy In the treatment of teratomas of the testicle, however, the question becomes one of whether operation should follow Α Randall and A irradiation Bothe¹⁵ state that in teratomas of the testicle simple orchidectomy has given less than ten per cent cures, radical orchidectomy with removal of regional lymph nodes-19 per cent cures and x-ray therapy alone 29 per cent cures The authors point out that because of

the high frequency of differentiated radioresistant cells in teratomas, orchidectomy should follow all irradiation regimes. The radiation should include the entire body above the primary lesion, they say, to pick up any early metastatic radiosensitive cells.

Carcinoma of the Prostate—Carcinoma of the prostate is a prevalent type of malignancy and is too often considered moperable H H Young¹⁶ quotes the extensive postmortem investigations of Rich and of More to establish its frequency The incidence was between 14 per cent and 21 per cent in a large group of autopsied men past middle age It was found that nearly three-fourths of the cancers occurred in the posterior lobe Many of these growths were intracapsular, indicating that radical removal may have been possible The author points out that frequent rectal exammations would disclose these small areas of induration within the gland Operative exposure through the perineum is advocated making possible visual examination of the gland and frozen section if necessary to determine malig-The coexistence of obviously benign soft nodules does not rule out carcinoma, since in half the cases of prostatic cancer there is also present benign hypertrophy. If the growth is very small the author performs hemiprostatovesiculectomy. If such a removal is deemed inadequate the total radical operation is done through the perineum This includes removal of a portion of the membranous urethra, the entire prostate completely encapsulated, and in one piece the seminal vesicles, vasa deferentia, a cuff of bladder and a large portion of the trigone The author has done the radical operation in 61 cases There were seven hospital deaths, 17 cases with apparent cure and a large number who died without evidence of disease With this low mortality and moderate rate of cure, the practice of routine palliative prostatic resection should indeed be subject to revision.

General Considerations-Much has been written of the technical treatment of cancer. Occasionally there appears a work embodying certain general considerations of extreme importance which emphasize the care of the patient Such a discussion may be imbued with certain quasi-philosophical points but is essential none the less for an understanding of the full and complete treatment of the patient with cancer E E Downs, H Wammock and R T Artman¹⁷ separate their discussion into four headings (1) mental hygiene, (2) physical hygiene, (3) pain and (4) irradiation They further divide their cases into the curable and the advanced

Under mental hygiene the authors evaluate each patient as an individual problem, and attempt to estimate his emotional status If the patient is emotionally stable they have found that better cooperation is enjoyed if the patients knows that he has cancer On the other hand in fearful individuals it has proven advantageous to withhold the truth Everyone is agreed that the family should be informed of the true state of affairs, and that it should be made clear that cancer is not contagious. The family physician should always be in close touch with the course of a patient's treatment under a specialist. He in turn should keep the family intelligently advised, and the patient optimistic and encouraged-an undertaking of no small proportions

Physical hygiene is largely a problem of nursing care Nurses should be trained in the ways of tumor growth. The authors in addition recommend a high caloric diet rich in vitamins. Reinforcement with insulin, iron and alcoholic

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beverages is often helpful Many cancer patients become emaciated simply because they are not fed enough Nasal catheter feedings are essential in nose and throat carcinomas especially during the irradiation reaction. The patient should be kept up and about as long as possible. This keeps up the morale, aids metabolism and lessens pulmonary Physical and occupacomplications tional therapies are recommended The authors suggest daily bicarbonate tub baths in patients with large granulating surfaces Dakins' solution and potassium permanganate are invaluable in sloughing or infected wounds In cases with mouth lesions, tooth hygiene is very important and unsound teeth are best extracted if such is possible

Treatment of pain, as Auster is quoted, depends upon knowledge of its origin Pain may arise from local nerve involvement or it may be central Pain is not of such great moment in the curable case, but in the advanced case fine judgment is frequently necessary in the selection of drugs for its relief Before resorting to narcotics all other means of relief should be exhausted Here surgery often has something to offer Short circuiting gastric and intestinal operations may give untold relief from pain Transurethral prostatic resection, tracheotomy and urethral transplantations are listed by the authors as having a place in palliation

The relief of pain by neurosurgical means may be divided into five procedures Subarachnoid alcohol injections, alcohol injections of peripheral nerves, chordotomy, division of peripheral nerves and pelvic sympathectomy. Subarachnoid alcohol injections are safe and effective Chordotomy or cutting of the anterolateral columns of the cord requires the technic of an experienced neurosurgeon. All these pro-

cedures, according to the authors, give good results when applied to the proper cases

Frequent dressing and careful cleansing of ulcerated wounds can do much to relieve local pain. The selection of the drugs depends upon the severity of pain. Salicylates and coal tar derivatives should be exhausted first Combinations with codeine are usually effective. Dilaudid, pantapon and morphine cover the more potent narcotics. Scopolamine has a terminal use

The authors state that in the advanced case, small doses of x-ray will do much to relieve pain After such irradiation extensive ulcerations may Pain from skeletal metastases is relieved frequently by deep x-ray Roentgen castration of the menstruating woman with breast cancer sometimes relieves pain from osseous metastases Calcium intravenously or by mouth may be of some use. The authors recommend in general therapy the preoperative irradiation of a malignant tumor to gauge its sensitivity, to reduce its size and to lessen the likelihood of metastases Frequent blood counts are necessary in patients under an irradiation regime If the white cells drop below 2000 or the hemoglobin below 50 per cent active measures are instituted to increase the count Transfusions, iron and liver are of value Irradiation sickness is combated with subcutaneous glucose and saline in severe cases The authors give all cases receiving intensive irradiation 10 mx of viosterol and 6 to 8 oz of orange juice with sugar tid

Brain tumors require especial caution against overdosage with resultant increased intracranial pressure. This complication is treated with 50 per cent glucose intravenously or decompression. The patient or family should be instructed to expect such complications as

epithelitis and secondary skin changes The radiologist should be fortified with biopsy and serial pictures of the lesion if possible.

Prognosis — A Graham¹⁹ reasons quite properly that histologic grading, although indicative of the inherent malignancy of breast cancer, is not the most important determining factor in its prognosis. He states that prognosis in treated cases is more closely concerned with the degree of localization, or the extent and character of the involvement review of some 640 cases of breast carcinomas operated in the Cleveland Clinic between 1896 and 1930 comprises the basis for this opinion. After exclusion of the papillary and sweat gland caremomas as well as cases with madequate records there remained 545 cases tor analysis. The criteria used for groupmg these cases were applied to the gross specimen after operative removal. They were designed to determine the extent of the lesion and enabled the breasts to be segregated into four groups

Group I—Those in which the histological diagnosis of cancer was made in the absence of gross tumor There were only 12 such cases and none died with evidence of cancer

Group II—Those showing local tumor without axillary metastasis or other signs of extension.

Group III—Those showing local tumor with only early or moderate axillary involvement

Group IV—Those displaying certain signs of incurability such as diffuse infiltration, secondary nodules in the breast, skin or muscle, edema of the breast or skin, extensive axillary metastasis, and metastasis to the supraclavicular nodes or to distant parts

In Group I none of the cases died of cancer before or after the five-year post-operative period. Forty-two per cent of the 161 cases of Group II, 89 per cent of the 150 cases in Group III and 100 per cent of the 222 cases in Group IV were known to be dead of cancer before or after five years. In the Reviewer's opinion this method presents a rational means of prognosis in breast cancer removed by the radical operation.

D C Balfour²⁰ discusses the factors upon which prognosis in gastric cancer depend. He states that cancer is the commonest of the organic diseases of the stomach In the Mayo Clinic between 1906 and 1931, 4793 cases of gastric carcinoma were operated upon operative mortality in this group was 94 per cent, over two-thirds of the group having had either partial or complete gastrectomy. The two chief causes of postoperative mortality were peritoritis and pneumonia. In the larger operable lesions the expectancy of life was greater than in the smaller probably because of earlier discovery and lesser penetration proximity of the lesion to the pyloris made the prognosis poorer, because as the author states, it is more difficult to remove the entire lymphatic drainage In this series when the entire growth and regional lymphatics could be removed completely, the five year cures

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reached about 30 per cent. When the removed nodes in these cases were found to contain tumor the five year cures were 18 per cent and when no node involvement was found the cures reached 48 per cent Five year survival percentages were greater in older than in younger patients

The interpretation of statistics on cancer morbidity and mortality from census and insurance company reports is difficult The accuracy of the data is sometimes questionable due largely to difficulties in diagnosis. The results of these statistical analyses, however, are largely valid L I Dublin,21 after review of the US Census Bureau reports and those from other sources, states that malignant disease accounts for 150,000 deaths per year This is outranked only by deaths from heart disease. At the present rate in initial groups of 100 white people the author calculates that ten males and 13 females will ultimately die from some form of cancer The following statements are based upon some 17,500,000 policy holders in an insurance company Carcinoma has advanced from seventh place 25 years ago to second place at present in the listed causes of death This is due to declining death rates in other torms of disease. There has been an increase in the death rate from cancer of 145 per cent in 25 years and this is due to the increased male deaths and not temale. In white females the rate has declined According to organ involved one half the fatal cancers are in the digestive tract. Cancer of the female breast and genitalia account for 30 per cent and of the skin and other organs 20 per cent The trend of mortality in cancers of the genital organs in white females is downward but the death rate from cancer of the female breast has increased The author states that "Cancers of the buccal cavity are about seven times as frequent in white males as in white females," but the trend of the death rate from this site has been downward.

The question presenting itself to the REVIEWER is whether the recent downward trend in mortality from cancers of the genitalia of the white female and of the buccal cavity in general is not due to increasing curability of these cancers by irradiation

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GYNECOLOGY AND OBSTETRICS

By P. Brooke BLAND, M D, and ARTHUR FIRST, M D

GYNECOLOGY

Introduction — Conservation is the keynote of modern gynecology and obstetrics. In the former specialty more and more is the trend away from operative intervention in the treatment of malignancy and toward radioactive therapy

Functional menstrual disorders are now thoroughly investigated from the endocrine standpoint and satisfactory treatment is being evolved as a result Sterility has become a scientific specialty and many barren marriages have resulted in the birth of offspring as a result of advances in this field. Trichomonas and monilia infestation of the vagina still have a host of therapeutic drugs advised attesting to the fact that complete cure is often difficult and prolonged.

In obstetrics it is evident that most effort is being expended toward a reduction in maternal and fetal morbidity More caution is being and mortality urged in the injudicious use of analgesics and in anesthetics in labor, as maternal deaths are being reported as a result of the insistent demands of the patient for painless childbirth. The complications of pregnancy and their treatment receive special emphasis this year A more conservative attitude in the treatment of eclampsia is evident. The advantage of low cervical cesarean section is now an accepted fact

MENSTRUATION

Experimental Data—S Zuckerman¹ observed that the administration of 25 mg of testosterone propionate twice a week to normal mature female rhesus

monkeys stopped the menstrual cycle during the period of injections (up to seven months) The internal reproductive organs were not injured by the treatment, and in one animal menstruation recurred about a week after the last injection Follicular growth and luteinization were both inhibited. Apart from enlargement of the clitoris, no other significant clinical changes occurred. It is suggested that testosterone propionate may be of clinical value for the induction of temporary sterility and the control of uterine bleeding.

Artificial Menstruation Following Hysterectomy

Treatment—O T Roberg, Jr,2 outlines an operation for prolonging menstruation following hysterectomy procedure consists in transplanting a piece of the mucosa of the removed uterus into either the vaginal wall or the cervical stump and is successful in the majority of cases This artificial menstruation has a pronounced psychic value and may serve to postpone the physiologic menopause, which seems to occur at an earlier age than usual in cases of simple hysterectomy. The operation provides an experiment in which menstruation is continued by a comparatively minute portion of the uterus It is thus an objective demonstration of the extent and regularity of menstrual function in the absence of the greater part of the uterus, and it leads to conclusions which may support the theory that the uterus plays an important primary part in the function of menstruation Endocrine therapy in an attempt to revive transplant bleeding when it has ceased may serve to support the view that the activity of the transplant is dependent on ovarian activity.

Amenorrhea

A thorough study of 27 patients with amenorrhea is reported by R. T. Frank, M A Goldberger, U. J Salmon, and G Felshin ³ Of these six were primary in which menstruation had never occurred and 21 secondary amenorrheas

By all available clinical criteria determined as a routine before selecting the patient, including the secondary sex characters, basal metabolism, blood examinations, sellar x-ray films, Janney test for sugar tolerance, blood pressure, pelvic examination, and the like, 24 of the 27 patients showed no serious deviations from any group of normal women of similar economic and social status. In the great majority the sole complaint was the amenorrhea

Complete estrogenic determinations, extending at least over one month, were made on 21 patients In several, these determinations were repeated In ten, both estrogenic and gonadotropic determinations were made, including weekly blood specimens for the determination of both the estrogenic and the gonadotropic factors, as well as continuous urine examination over 30 days of estrogenic and gonadotropic factors. In six, only estrogenic and gonadotropic blood determinations were made In six. gonadotropic urine determinations were performed

Of 27 amenorrheic patients investigated, both primary and secondary, five were studied for less than one month, the remainder for from one month to more than one year

The ages varied from 20 to 37 years Of the 18 married patients, 16 were sterile

The amenorrhea had existed from five months to nine years in the secondary group; the primary group (six patients) were from 23 to 33 years of age.

Twenty-four of the patients showed no endocrine stigmas; three had hirsuties and of these two had enlarged clitorides.

Urinary Excretion of Estrogens

In 21 cases complete studies of the urinary excretion of estrogens were performed for more than one month. The patients fall into four groups:

- (a) Low—From 50 to 100 mouse units total monthly excretion. There was no positive estrogenic reaction in 40 cc. of blood in any. Seven cases.
- (b) Subthreshold—From 500 to 518 mouse units excretion. Two showed estrogen in blood Five cases
- (c) Normal Excretion—From 1000 to 1714 mouse units Four showed some estrogen in blood. Six cases
- (d) Excessive Excretion—From 2075 to 2328 mouse units All showed estrogen in blood. In their series this group (Zondek's "polyhormonal amenorrhea") is less numerous than anticipated

In ten cases complete studies of the urinary excretion of gonadotropic substances were performed for one month or more. These patients fall into two groups

- (a) High and Continuous Gonadotropic Excretion—Four cases All four estrogenic groups were represented (see 5 a, b, c, d)
- (b) Absent Gonadotropic Exerction— Six cases Again all four estrogenic groups were represented

The gonadotropic blood and urine studies cannot be correlated to the estrogenic conditions, thus differing both from normal women in whom the blood and urine show preovulatory accumulation and from patients in the menopause in

whom blood and urine show continuous and increased amount of gonadogens

The doses of estrogen given for therapeutic effect to amenorrheic patients varied between 16,000 and 690,000 rat units (80,000 and 3,450,000 international units) Below 200,000 rat units no response obtained Even with the large doses employed, a single uterine bleeding followed in only two and scant spotting in two Approximately one-tenth of the estrogen given is excreted in the urine

Gonadotropic substances (extract of pregnant mare's serum, anterior pituitary gland extract) in dosage of from 60 to 510 rat units produced no effect

In contrast to the foregoing groups were patients afflicted with obesity, malnutration and hypothyroidism, who uniformly responded to appropriate therapy

Finally, attention is drawn to the considerable number of patients in whom menstruation returns without any treatment or ascertainable cause

The author concludes that in amenortheic women a wide variation in the hormone status occurs

Evidence of almost complete ovarian atunction subthreshold function and normal follicular activity as well as excessive activity are represented

In these tour groups the gonadotropic assay may show either overfunction or underfunction

No evidence pointing to either a primary pituitary or a primary ovarian causation of amenorrhea could be demonstrated

Amenorrhea does not preclude the occcurrence of ovulation or pregnancy

The response to estrogenic therapy of amenorrheic patients differs markedly from that in the menopause

The threshold of response in amenorrhea is far higher than in the menopause

This difference can be utilized in patients to differentiate between the two

conditions, if an excess of gonadotropic substance has been found in the urine Disappearance of gonadotropic substance produced by 30,000 rat units of estrogenic substance warrants the diagnosis of menopause

No useful purpose is served in prescribing estrogens for the treatment of amenorrhea

In the dosage used by us, gonadotropic preparations likewise proved ineffective

It is justifiable to try very high dosage of gonadotropic preparations when these become available

Their study has failed to locate the cause or causes producing amenorrhea.

Dysmenorrhea

Sixty cases of functional sterility were selected as suitable for endocrine therapy by J. Kotz and E. Parker ⁴

In selecting cases of functional dysmenorrhea for study the following classification was used

Classification-

- I Dysmenorrhea caused by Organic Pathology
 - 1 Pathology of the genital organs
 - 2 Constitutional abnormalities
 - 3 Combined local and constitutional abnormalities
- II Dysmenorihea caused by Functional Pathology
 - 1 Nonendocrine causes
 - (a) Pelvic congestion
 - (b) Allergy
 - (c) Neurosis
 - 2 Endocrine causes
 - (a) Ovarian dystunction, primary
 - (b) Ovarian dysfunction, secondary
 - (1) Hypopituitary function
 - (2) Hypothyroid func-

Treatment—Based on the concept that dysmenorrhea may be due to an imbalance between theelin and progestin production, therapy should be directed toward a reestablishment of the normal ratio of these hormones. Theoretically, this could be accomplished either by supplying the deficient hormone or by stimulating the glands to secrete normally Organotherapy constitutes the first method, and x-ray accomplishes the second

In the use of organotherapy in the treatment of dysmenorrhea several products are to be considered, namely, the anterior pituitary-like hormone of pregnancy urine, the luteal hormone, thyroid, and theelin.

- 1 The anterior pituitary-like hormone is of questionable value, since it is doubtful whether this substance actually stimulates the human ovary to corpus luteum formation
- 2 The luteal hormone is marketed as proluton (Schering, in strengths of ½5, ½5, 1, 5 international units) and as progestin (Uphohn) Proluton is used purely as a temporary measure, since it is substitutional in its effects and cannot be expected to effect a permanent cure. It is given beginning two weeks preceding the expected period in doses of 1 cc containing one international unit, every other day up to the onset of the period. In severe cases the five international unit strength is used and is continued throughout the period.
- 3 Thyroid when indicated is a helpful agent
- 4 Theelin is definitely not indicated in the treatment of dysmenorrhea, except perhaps in the presence of an infantile uterus and even here the deficiency is better corrected by the stimulation of the pituitary gland
- 5 The use of the x-ray to the pituitary gland in functional disorders of the female given in fractional doses is more beneficial in the correction of functional disorders of the female than any endo-

crine preparation now available The technic of x-ray therapy is as follows:

"20 milliamperes, 200 k.v p, 5 minutes, 60 inches distance, ½ mm copper and 1 mm aluminum filter (170 'r' units) to right and left sides of the pituitary gland every three weeks for four treatments At the end of this, patients may return in two months and another series may be given if necessary."

Of the 60 cases, 53, or 88 per cent, were relieved, six, or ten per cent, were improved, and one, or two per cent, received no benefit from the treatment

OVULATION

Fertility and Ovulation

P Willson⁵ discusses recent evidence that fertilization of the ovum is possible only for a period of less than 24 hours in any menstrual cycle Fertile intercourse, therefore, must occur not more than 24 hours before ovulation

This view is revolutionary and runs counter to the conclusions drawn from the more or less continuous sexual activity of man and the primates as opposed to lower animals. Furthermore, it conflicts with the previous understanding of the biologic analogies of human menstruation.

At present, no practicable method or methods exist for exactly timing ovulation. In the present state of knowledge it seems wise in the attempted determination of the date of ovulation to allow two days before and two days after the theoretical date. This results in placing its occurrence somewhere in a five-day period covering inclusively the twelfth to the sixteenth day before the beginning of the next menstrual period. It is necessary to add two days before the twelfth to cover the term of functional activity of the sperm and one day

after the sixteenth to allow for the death of the egg The period of possible fertility is further lengthened in most women by the fact that the menstrual cycle is likely to vary at least a few days in either direction. Thus, assuming a cycle varying between 26 and 30 days (actually few will be found more regular than this) the theoretical date of ovulation using the shortest cycle of 26 days may be estimated at the twelfth day after the day the last period began Four additional days before this must be allowed two for possible occurrence of early ovulation and two to cover the span of viability of the sperm. This calculation places the first day of the possible fertile period on the eighth day after menstruation If the patient were regular with a 26-day cycle, this day, the eighth, would be the first of a fertile period of eight days, made up of the four days previous to the theoretical day of oxulation, the day of ovulation itself, two days after this to allow for late ovulation, and one additional day to allow for death of the egg. In view of the irregularity of the cycle, however, the difference of four in this instance is now added to the eight days originally figured to make a total of 12, the number of days of the possible fertile period in this particular patient Practically then, the average woman with a maximum irregularity of five days who follows this method of birth control must observe a fertile period of 13 days which, in addition to the days of menstruation makes her incapacitated for marital relations for 18 days in each menstrual cycle Put in another way, this woman must abstain from intercourse 234 days in each year, as against 65 days necessary for the one who is using adequate modern contraceptive measures

The "safe period" according to the author, when determined by a competent physician or intelligent layman on reli-

able menstrual data, is believed to be as reliable as any other known method of contraception. It is, however, unpractical for a considerable proportion of women and unworkable for some and is therefore in no sense a uniformly satisfactory method

SEX

Diagnosis in Utero—The diagnosis of sex of the human fetus *in utero* is thoroughly reviewed by S B Blakely ⁶ The natural means to diagnose fetal sex may be divided into three groups, namely:

Group 1—The supposed origin of the male from the right side of the uterus, the female from the left, and the changes in the right side of the pregnant woman's body ascribed to, or imagined to result from, such origin

Group 2—The position, outlines, attitude and activities of the fetus during pregnancy and labor

Group 3—The effects of a male fetus on the total maternal organism, $i\ e$, the reactions of the female body to the introduction therein of a male element. This is the largest and most important group

Group 1—Schoener holds, that the right and left ovaries alternate continuously in their activities (an idea suggested by Dischoff in 1844), that the human ovum possesses its sex "Anlage" before fertilization, and that the sex "Anlage" changes, possibly better said, appears, in each ovary in the following sequence right ovary, male, left ovary, female, right ovary, male, left ovary, female, right ovary, female, left ovary, male The cycle is repeated ad infinitum Rumley Dawson proposed the hypotheses that male and female determining ova are discharged from the ovaries alternately, male from the right and female from the left Both these men claim

that, after the first pregnancy, it is possible to quite accurately foretell the sex of future children by a careful history of the menses (actual and missed), assisted by the palpation of an enlarged tender ovary due to the presence of the corpus luteum of pregnancy The difficulties of these theories are quite apparent, e g, menstruation is not always associated with ovulation nor vice versa. and the sex of children after unilateral oophorectomy does not always conform to the rules Through many years of observing pregnant women, the author has never been able to determine any right-sided signs or symptoms peculiar to a male pregnancy, nor evidence of either definitely alternating ovarian activity or of the ovular determination of sex It is probably safe to deny their existence, though dogmatic statements about the physiology of sex are dangerous

Group 2-In this group belong two modern "natural" means that have been employed in the effort to solve the problem the x-ray (two procedures) and the rate of the fetal heart Roentgenologists agree that the ossification of the skeleton of the female is more advanced than that of the male throughout intrauterine life, it has been suggested that this fact might be utilized to foretell fetal sex Visualization of the fetus in utero (including the outlines of the soft parts) by rendering the amniotic fluid opaque through the injection of strontium iodide into the amniotic sac, occasionally permits the diagnosis of fetal sex, if a true lateral view of the breech is obtained (menees)

In 1859, on the basis of a study of 100 cases, Frankenhaeuser suggested that fetal sex might be determined by the rate of the fetal heart in the last three months of pregnancy, a persistently slow rate (averaging 124 or less a minute)

indicating a boy, and a persistently more rapid rate (averaging 144 or more a minute) a girl. A large number of observations have been made with a corresponding literature. If the male fetal heart is slower, it must be due to some peculiar influence of male sex itself, maleness per se, for which the author knows of no evidence, or because the male is heavier or bulkier, but the average difference in the birth weights of the sexes would seem to be too slight to have much effect, or the result of some hormonal action, as yet unknown

Group 3—In pregnancy, mother and child are a biologic unit. If the mother's own hormones produce well-recognized phenomena, why may not added fetal hormones (which she surely receives) alter these phenomena in degree or character?

The idea that the reaction of the pregnant woman to a male fetus is qualitatively different than to a female fetus, is very old. Does the introduction of maleness, cg, a male fetus, into the female body produce quantitative or qualitative changes that can, possibly one might add, some day in the future, be recognized by the clinician or the laboratory worker? Is there any evidence that a male pregnancy has an effect on the mother, different in degree or character from that of a female pregnancy?

The reviewer feels justified in the conclusion that the introduction of the male element into the female body does produce effects. The mechanism by which the male fetus is protected against the antagonistic sex hormones of the mother is, at times, more or less broken down. Sufficient means and knowledge are not yet at hand to definitely recognize such effects and permit practical sex diagnosis.

Although fetal sex hormones must be the primary cause of any differences

that may exist in the effect of fetal sex on the pregnant woman, endocrinology to date has disappointed high hopes of solving the problem of fetal sex diagnosis. The male and female sex hormones are closely related chemically, their differentiation in the blood is difficult, and "both male and female stimulating substances can be extracted from both male and female urines"

The reviewer concludes that the correct prognostication of fetal sex would satisfy a great curiosity and answer the pregnant woman's age-old question It is true that it would not have great practical value Research along other lines might well produce more solidly beneficient results It may be true that such diagnosis, if possible early in pregnancy, might increase the incidence of induced abortions, though this does sound a bit timorous and farfetched The parents made unhappy by knowing beforehand what they were going to have might easily be outweighed by those rejoicing in the knowledge that they would have a child of the sex they most desired. Its discovery might be exploited by the unscrupulous, as was salvarsan in its early history. All these and other objections have been raised But the fact remains that no permanent harm has ever come by making the way of truth wider or smoother or straighter, or by pushing it a little farther diagnosis of fetal sex in utero is one of the unsolved problems of obstetrics

MENOPAUSE

Treatment by Irradiation of Pituitary—R Zollinger and W W Vaughan⁷ employed irradiation of the pituitary body in the treatment of 14 women who complained of varying degrees of discomfort during the menopause. The majority were having severe symptoms. At

least one-half of these patients had taken various kinds of ovarian preparations and sedatives with little or no benefit. Most of the patients selected for treatment complained of insomnia because of the hot flashes, accompanied by marked perspiration

The menopause followed surgical castration in seven patients, roentgen therapy in four and application of radium in one, and was of natural occurrence in the remaining two cases The duration of symptoms, before radiation therapy was instituted, varied from two months to eight and one-half years Of the 14 patients treated at least nine months to one year ago, five had a definite and sustained decrease in the number of hot flashes and marked symptomatic improvement; three other patients stated that they were definitely improved, although by tabulation there was little if any change in the number of hot flashes The remaining patients were not improved subjectively, and the number of hot flashes remained at a preirradiation level The patients showing definite improvement recorded a fall in the number of hot flashes about the third day of therapy

Although a standard of from 1400 to 1600 roentgens was given over a period of four days, this quick response may be taken as an indication that benefit could be expected from smaller doses, such as 800 roentgens. To rule out the psychic effect of x-ray treatment three patients were given sham therapy, two reported a decrease in the intensity of the flashes Three of the five patients who were definitely improved had had castration by surgery within a year of the onset of treatment The average age of the improved patients was 36, which is six years below the average for the entire group Basal metabolic and sugar

tolerance determinations were made before and at intervals after the irradiation in order to check any possible damage to the diabetogenic and thyrotropic hormones, but there was no remarkable deviation from the preirradiation studies In two of the cases there was a slight flattening of the sugar-time curve, which was not extreme enough to be more than Biopsies of the vaginal coincidental mucosa were obtained in ten patients The specimens obbefore irradiation tained prior to irradiation corresponded ın all respects to postmenopausal vagınal mucosa No definite change after irradiation could be found, even in patients showing marked clinical improvement

UTERINE HEMORRHAGE

Treatment—Of 12 cases of juvenile gynecologic hemorrhages in which P Caffier's resorted to *irradiation of the spleen*, nine cases responded favorably. In four of them the improvement was only temporary. However, in four of the five cases in which the treatment was most effective, not only was the hemorrhage arrested in from one to three days but the menstrual cycle became more regular.

The author directs especial attention to the value of irradiation of the spleen in hemorrhages caused by myoma. Irradiation of the myomas often fails to produce prompt cessation of the hemorrhages, while the irradiation of the spleen quickly effects hemostasis, probably by mercasing the coagulation ferment view of its rapid action, simplicity and harmlessness, he advises irradiation of the spleen for hemorrhages caused by myoma in patients in whom the removal of the invoma is contraindicated. Irradiation of the spleen need not be restricted to cases of myoma but can be used also in refractory climacteric hemorrhages provided the essential cause of the hemorrhage is excluded by other methods.

Postmenopausal Hemorrhage

Diagnosis—By examining the records of all the patients (349) entering the Johns Hopkins Hospital with postmenopausal bleeding between January 1, 1919, and January 1, 1935, in which complete pathologic and clinical data were available, R W TeLinde9 hoped to determine the pathologic lesion causing the condition The most frequent lesion responsible was carcinoma of the cervix, which occurred in 324 per cent If the cases of carcinoma of the cervix are added to those of the body of the uterus (149 per cent), it is found that the cause of postmenopausal bleeding is due to cancer of the uterus in 473 per cent. If to this are added the other malignant growths (11 cases of malignant ovarian tumors, five cases of sarcomatous change in myomas, three cases of sarcoma of the endometrium and one case each of sarcoma of the vagina and secondary carcinoma of the vagina), a total of 533 per cent of the cases of postmenopausal bleeding are due to malignant changes of the genital tract Therefore every woman bleeding a year or more after her menstrual period has more than an even chance of suffering from some malignant process warrants the demand for a complete diagnostic study of all such patients. It is impossible to guess as to the malignant or benign source of the bleeding from the amount or character of the bloody discharge. Some of the cases with the least bleeding proved to be due to malignant lesions, while in others the most profuse bleeding was due to benign lesions Bimanual and speculum examinations should be a routine procedure in every case When these measures fail to reveal the cause, a diagnostic

curettage will establish the diagnosis in most instances. On following a patient with postmenopausal bleeding in whom these diagnostic measures have failed to reveal the cause, one should regard an increase in the size of an ovary, suggesting beginning neoplasm, as an indication for a laparotomy.

Functional Uterine Hemorrhage

Treatment—The treatment of functional uterine hemorrhage is reviewed by F E Keene and F. L Payne 10 This may be divided into seven groups: (1) Hygienic measures. (2) Uterine stimulants. (3) Means to increase the coagulability of the blood or to decrease the permeability of the capillaries. (4) Endocrine therapy. (5) Removal or destruction of the endometrium (6) Roentgen or radium therapy. (7) Surgical procedures upon the ovaries or the uterus

- I Hygienic measures are of value when used in conjection with appropriate medical and glandular therapy. Constitutional defects often are attended by disturbances in endocrine function which are expressed by abnormal uterine bleeding. A common experience is the frequent alteration in menstruation with either the development of abnormal hemorrhage or a return to normal periods which follows a change in vocation climate, or environment.
- 2 Uterme Stimulants—Various uterme stimulants have been recommended in abnormal uterme bleeding under the assumption that it is due to faulty contractibility of the uterme muscle incident to malposition, chronic subinvolution, or inherently poor muscle tone Ergotamine tartrate, extracts of hydrastis, stypticine, pituitrin, adrenalin chloride, breast stimulation, by galvanic stimulation, intravaginal

ultraviolet therapy are all recommended for certain cases.

3 Blood Coagulants and Endothelial Stimulants—Substances which affect the coagulability of the blood or the permeability of the capillary walls have been added recently to the list of therapeutic agents in functional bleeding Moccasin venom was introduced by Peck and Goldberger in 1933 believes that the results are due to changes in the vessel walls or to some effect upon the clotting factors of the The technic of administration consists of the subcutaneous or intramuscular injection of the 1 to 3000 dilution of moccasin venom The initial dose should be 05 cc, increased to 1 cc by the third day As much venom as possible is administered during the first ten days, because sensitivity necessitating desensitization often develops at the end of that time Daily injections of 1 cc are given during the active bleeding to be decreased to two or three injections a week after the bleeding is controlled Recurrences, which are frequent, usually respond to the second series of injections treatment should be continued through three menstrual periods

Cevitamic acid, which is the active principle of vitamin "C," has been used in German clinics for some time. Fifty milligrams of cevitamic acid approximately corresponds to the active vitamin "C" in 100 cc of fresh orange juice. Marked deficiency in vitamin "C" results in scurvy with its hemorrhagic manifestations. It seems that cevitamic acid acts upon the blood and the blood vessels. The technic of administration consists of the daily intramuscular or intravenous injection of 50 mg of cevitamic acid in an isotonic saline solution. According to the reports, this usually

checks profuse uterine bleeding within four to six days.

Intravenous injections of Congo red have been used for the control of venous bleeding of various types, including uterine hemorrhage. The recommended dose is 5 to 10 cc of the sterile isotonic solution administered intravenously. A single injection often checks the bleeding or several injections may be necessary at two- to three-day intervals

The clinical use of parathyroid extract, which is usually given in conjunction with calcium, was made practical by Collip While the immediate effects are usually good, recurrences are common, rendering parathyroid extract ineffective as a curative measure

Blood transfusions are often of value in the treatment of severe functional bleeding. Not only do they combat the anemia, but in some instances they are curative in that cessation of bleeding and a return to the normal menstrual flow may follow a single transfusion.

- 4 Endocrine Therapy Since functional bleeding is caused by abnormal endocrine activity, practically all of the glandular products have been given a trial in its treatment *Estrin therapy, corpus luteum extracts, thyroid therapy,* the *anterior pituitary-like hormone* are all recommended with good results
- 5 Destruction or Removal of Endometrium—The modern conception of the causes underlying functional bleeding would seem to cast discredit upon curettage and other methods of removing the endometrium, but the fact remains that satisfactory results have been reported from the use of such measures

The authors experience with curettage has been disappointing. Whatever benefit may accrue is temporary, recurrences taking place in more than half of the cases within two months.

6 Irradiation — Irradiation has become a widely used method of treating functional hemorrhage and in patients of the menopausal age pelvic irradiation approaches the ideal. It is also of value in women of less mature years, but it must be used with the greatest caution because of its effect upon ovarian function. Roentgen irradiation has been applied to the pituitary gland, the spleen, and the ovaries, alone or in combination

The most common form of irradiation therapy is that applied to the ovaries and uterus and when properly used, this is a safe and effective method of treatment. Its harmful effects depend upon disturbance in the secretory function of the ovaries and in alteration of the ova so as seriously to affect subsequent pregnancy

Radium Therapy—The authors prefer radium because its dosage can be regulated more delicately and the beneficial effects are in part due to its local action upon the uterine blood vessels. Further, with radium, completion of the treatment is accomplished at the time of the diagnostic curettage which should precede either form of irradiation in most instances.

Profoundly anemic patients react poorly to both radium and roentgen therapy and either form of irradiation should be withheld until the blood has been improved by transfusion and other appropriate treatment

Technic of Application—The authors prefer general anesthesia because it permits a more accurate pelvic examination. The uterine cavity is explored with a sound and a curette in order to eliminate an organic lesion such as retained secundines, pedunculated submucous tumors, or carcinoma. The length of the uterine cavity is measured and 50 mg of radium, filtered with 1 mm of platinum, is encased in a soft rubber tube 2 mm in thickness and of a length

corresponding with that of the uterine cavity The radium should be in the top of the uterus In order to prevent slipping of the rubber tubing, the external end is sewed to the anterior lip of the cervix as advised by Furniss. As an added safeguard, the vagina is packed. When the radium is to be in place for eight hours or more, a permanent catheter is placed in the bladder The patient remains in bed for two or three days and is usually sent home on the fourth In properly selected cases, the intrauterine application of radium is attended by no mortality and a minimum of morbidity Nausea and vomiting commonly occur so long as the radium remains in the uterus, but they rapidly subside with its removal

Dosage—The initial dosage of radium is of paramount importance. This decision depends not only upon the incidence of controlled bleeding which can be anticipated from a given dosage but also upon the incidence of amenorrhea and severe menopausal symptoms which may follow this dosage.

Radium is rarely indicated in the treatment of patients under 20 years of age. When it is found necessary, the initial dosage should not exceed 200 mg hours.

Between 20 and 30, the authors' results show that a dosage of 400 mg hours can be administered sately. This dosage will be more than 80 per cent efficient in the control of bleeding, but a few patients will develop a temporary amenorihea of a few months' duration. Should the bleeding persist, the dosage can be increased by 100 mg, hours.

Analysis of the group between 30 and 40 brings out the important fact that with increasing dosage there is a rapidly increasing incidence of menopausal manifestations. With a dosage of between 800 and 1200 mg hours, permanent

amenorrhea occurred in 56 per cent and severe menopausal symptoms in 47 per cent of the patients. An initial dosage of 300 mg hours will control the bleeding in 80 per cent and without permanent amenorrhea. Should reradiation be necessary an application of not more than 400 mg hours should be administered and if this fails, the authors favor hysterectomy with conservation of ovarian function rather than increased irradiation

Functional bleeding occurs most frequently between 40 and 50 years of age. and because these women are approaching the time when, in the normal course of events, functional activity will cease, the administration of a menopausal dose of radium has come into common usage. Keene and Payne believe this is a mistake because of the high incidence of severe menopausal symptoms In women near 40, they are using a 400 mg hour dosage Should this and a reradiation dosage of 500 mg hours fail, a hysterectomy is advised. In women near 50 years of age, increased radium dosage can be used because the incidence of severe menopausal symptoms attending it will more nearly approximate that of the uninduced menopause

Between 50 and 60 years of age, the results of radium therapy approach perfection. Maximum dosage can be given, since severe menopausal reactions rarely develop.

Menorrhagia

Treatment—The treatment of functional menorrhagia and metrorrhagia is discussed by J C Burch, G S McClellan, J W Simpson, C D Johnson and E T Ellison ¹¹ In attempting to correlate the type of bleeding with the type of endometrium, one finds that no absolute relationship exists There is, however, a tendency for the minor disorders to occur in cases showing a more

or less normal endometrium, indicating a first degree ovarian failure

Whatever the degree of ovarian failure, a careful examination of the patient will usually reveal evidence of some endocrine disturbance The most common offenders are the pituitary, the thyroid and the ovary. Associated with the endocrine lesion one often finds such other conditions as anemia, focal infections, nutrional disturbances and nervous conditions.

The first and most important principle in the treatment of menorrhagia and metrorrhagia with *endocrine products* is an accurate diagnosis

The second principle is the treatment of the existing endocrine lesions with specific measures The most satisfactory results are obtained in hypothyroidism. A standard thyroid preparation is selected and administered in all such cases, thereby eliminating difficulties arising from variations in the strength of various extracts In the authors' experience it has been best to start with from 1/2 to 3/4 grain (003 to 005 gm) of USP desiccated thyroid daily. After a period of two weeks, the dose is adjusted according to the patient's response The adjusted dose is given for two weeks and the procedure repeated. The basal metabolism is determined at the end of six weeks and the dose of thyroid is increased until the metabolism is at or near normal, or until undesirable symptoms occur such symptoms do occur, the dose is reduced to the level at which the greatest effect can be obtained with the least undesirable reaction

Any of the accepted gonadotropic products of pregnancy urine or of the placenta are useful in the treatment of abnormal uterine bleeding resulting from hypothyroidism. Their effect, however, is transient, since the underlying hypothyroidism is not permanently influenced by their use. In primary ovarian disease

the preparations are extremely valuable, since direct stimulation of the ovary is produced. While the patient is bleeding, from 100 to 500 rat units of the gonadotropic substance may be administered daily until the bleeding ceases. This should be followed by weekly injections of from 200 to 500 rat units. If it is impossible for the patient to be seen at frequent intervals, single massive doses are often effective.

Progesterone therapy for the direct replacement of ovarian insufficiency due to absent or abnormal corpus lutem would seem to have much to offer Effective therapy with a few injections of from ½5 to ½ international unit (0.04 to 0.2 mg.) has been reported

In pituitary disorders there is often, in addition to the direct lack of pituitary secretion, a failure of the thyroid and ovary Pituitary preparations in the form of desiccated whole pituitary substance (60 grains, or 4 Gm., a day) or one of the injectable preparations containing the essential anterior pituitary principles (100 units daily) are used. These preparations are often not effective alone. In such instances small doses of desiccated thyroid, an estrogen or gonadotropic substance may be necessary as supplemental therapy.

The third principle in the treatment of menorrhagia and metrorrhagia with endocrine products is the eradication of factors contributory to the primary disorder. Foci of infection should be diligently sought and treated. The body weight should always be adjusted to the normal. Any anemia should be corrected. Snake venom is often effective as a stopgap, its hemostatic action allows the correction of anemia and gives an opportunity for other measures to take effect. The diet should be made adequate, especially in proteins and accessory substances, and rest and sleep

should be emphasized Neglect of this third principle is a frequent cause of poor results from good endocrine products

The final principle in the treatment of menorrhagia and metrorrhagia with endocrine products is the realization that surgery and irradiation produce only a symptomatic cure. However, they still have a definite and important place in treatment.

Uterine Bleeding

Treatment—The treatment of uterine bleeding with moccasin venom is reported by E J Davin, F Spielman and I A Rosen¹² who used it for parturient and puerperal bleeding. The injections of the venom were administered subcutaneously three times weekly to once daily and the dosage varied from 02 to 2 cc, of a 1 3000 solution in saline In the early cases the initial dosage was 02 cc, but due to the tendency toward localized skin reactions at the site of injections with this dose, the initial quantity given was changed to 05 cc Reactions in this way were almost completely eliminated Injections of venom were given either until bleeding had completely disappeared, as in the postpartum cases, or until parturition occurred as in the prepartum cases

In order further to check the results obtained, a fitth group consisting of 13 patients were given ergoklonin by mouth, one teaspoonful three times daily for ten days following delivery. The effects of the ergoklonin as compared to the snake yenom could then be evaluated

The period of puerperal bleeding in a group of 51 cases receiving snake venom injections postpartum was materially shortened as compared to the duration of bleeding in a group of 50 controls

The blood loss during parturition in a group of nine cases which received antepartum injections of venom was distinctly decreased in comparison to a group of 20 controls. Postpartum administration of the material also lessened the period of puerperal bleeding in these cases.

Puerperal bleeding was present in all but one of the 13 patients treated puerperally with ergoklonin for at least ten days after delivery

The mability to demonstrate the presence of antivenins in cord bloods obtained at delivery after prepartum injections of venom indicates that the material does not enter the fetal circulation.

No deleterious effects that could be attributed to the snake venom upon either mother or child were observed

The use of this material is recommended in the severe anemias as well as other bleeding conditions associated with pregnancy, and especially where a previous history of excessive hemorrhages in previous pregnancies is obtained

M A Goldberger and S M Peck¹³ report their results with the use of snake venom in functional uterine bleeding. The moccasin venom was used in a 1 3000 dilution with sterile sodium chloride (normal) containing 1 10,000 merthiolate. The venom was obtained through the courtesy of Dr. Raymond L. Ditmars of the New York Zoological Gardens. The dosage and the method of administration have been modified.

All injections were given subcutaneously. The initial injection was 0.5 cc and subsequent injections were rapidly increased to 1 cc (by the third injection). The interval between administrations of the venom depended on the severity of the bleeding. It was advisable to give as much venom as possible the first ten days, because at about that time the majority of patients developed a sensitivity to the venom which necessitated a decrease in the amount until desensitization was accomplished.

There was a distinct quantitative relationship between the desired clinical effect and the amount of venom given In cases with marked bleeding, 1 cc of the 1:3000 dilution was given daily or even twice a day until the hemorrhage was controlled In a number of the patients, daily injections were given at the beginning of the treatment. After the bleeding had been controlled the interval between injections of venom was increased so that only two or three treatments were given weekly

If the subsequent menstrual period approximated the normal, two injections a week were administered for at least three normal menstrual periods. During the course of the treatment a maintenance dose had to be established

In a number of treated individuals a period of from six months to one year of normal menstruation occurred after the venom therapy had been discontinued When metrorrhagia or menorrhagia recurred and venom was again administered, the initial dose was 1 cc If such a patient reported for treatment early enough, several l cc injections given two or three times weekly were found to be sufficient to bring about normal menstrual bleeding. It has also been noted that the course of injections necessary to control recurrences of bleeding was shorter than that necessary at the beginning of the treatment

STERILITY

Irradiation Treatment—The treatment of amenorrhea and sterility by radiation is reviewed by I I Kaplan ¹⁴. The reason for again calling attention to this mode of therapy is warranted because no other treatment so far devised, including organotherapy, has yielded satisfactory or equally good results. The enthusiasm aroused by endocrine studies

in this direction has so far led to disappointment. Many of the patients received irradiation only after prolonged endocrine therapy had proved unavailing. The present report is based upon a study of 128 married women who were referred to the author in private practice during the period of 1924 to 1936 for treatment of amenorrhea and sterility.

X-ray Therapy - In all instances treatment consisted of x-ray irradiation to the ovaries In 80 cases an additional treatment was given to the pituitary and in five instances also to the thyroid The factors used were 200 kv, 4 MA. with the filter of 0.5 mm copper and 1 mm aluminum, at a target distance of 30 to 40 cm Treatment was directed through four pelvic fields, 9 by 12, 10 by 15 cm, and to the pituitary area of 6 by 8 cm. The dose given was 75 to 150 r units (measured in air) per field at intervals, one treatment per week for three weeks Occasionally a fourth treatment was administered

Results-Of the 76 patients whose menstruation was re-established, 44 patients became pregnant. In 84 instances no pregnancy occurred Of the 44 patients who conceived, two are at present in the course of their pregnancy, 17 have conceived more than once, five conceived but aborted, two of these aborted twice Thirty-six patients became pregnant and went to term, giving birth to 47 living children and one stillbirth with an abnormal fetus Nine women have had more than one child There was one case of twins Of the 44 pregnant patients, amenorrhea existed from one month to 14 years, and sterility from one to 18 years. Only four patients had previously borne children, three had previously aborted or miscarried

None of the patients treated were harmed in any way. In no case did menstruction cease or become scanty where

menstruation had previously occurred in the usual manner

The 36 women who bore children received x-ray therapy to the pelvis and 18 received additional treatment to the pituitary. In two cases the thyroid was also treated

A study of the surviving children shows them all to be normal, both physically and mentally

Whether the x-ray affects directly the ovary, the uterus, or the pituitary, or is an indefinite endocrinologic factor stimulant, may be debated. Despite this the fact remains that it has been a definite factor in the successful treatment of the cases herein reported.

Dr I C Rubin in discussion of this report emphasizes the danger of an embryo being irradiated without the physician who sends the patient to the x-ray therapist being aware that the patient is pregnant. The treatment should therefore under no circumstances be instituted except within a week after a period no matter what the menstrual habit for that particular patient may be It a woman is irradiated who has had her period six, seven, or eight weeks ago although she menstruates habitually every four or five months, one may strike an carly period of gestation. The Aschheim-Zondek test in such instance can exlude the possibility of pregnancy

The results promised from endocrine therapy made Rubin abandon the radiation treatment for the time being, although he had had very good results up to 1929. Since that time he has used x-ray treatment in a few cases because hormonal therapy has proved ineffectual in this particular group. Experience has proved that the amenorrhea associated with sterility once being corrected is then followed by pregnancy in an appreciable number of cases

The difference between x-ray therapy and the more effective hormonal substances such as progestin and prolution is also of interest. There is no doubt that the menses may be induced by such hormonal therapy once, and even twice. and in an occasional case regular periods The x-rays induce menmay follow struation which becomes regular in the vast majority of the amenorrhea cases so treated There is no doubt that if we could obtain effective hormonal substance to correct deficiencies in function which we could definitely diagnose that then we should have reached the ideal in therapy. for the fear is still entertained by many that x-rays have a deleterious effect upon the germ plasm. In the children so far observed born of mothers who received x-ray treatment in fractional doses he has not observed any signs of degeneration which confirm the observations of However, there is still the Kaplan theoretical possibility that a third or fourth generation may exhibit stigmas traceable to such treatment

Diathermy Treatment-The treatment of obstructed fallopian tubes by diathermy and tubal insufflation is reported by M E Mintz 15 This report is based on the treatment of 44 cases of tubal obstruction as determined by tubal insufflation before treatment was started There were 30 cases of primary sterility and 14 cases of secondary sterility Of the 44 patients treated, patency was reestablished to some degree in 25 cases Of these 25 women, nine became pregnant and gave birth to normal children Two patients developed ectopic pregnancies necessitating operation instances no pregnancies have been noted as yet

Each patient received diathermy treatments one to three times a week, total ranging from 15 to 59 treatments Each

treatment lasted from 30 to 45 minutes, using from 2500 to 3000 milliamperes of current with the abdominal and sacral electrodes. When the abdominal and vaginal electrodes were used, the current employed was only 2000 to 2500 milliamperes. The electrodes used were a concave vaginal electrode, and for the abdomen and sacrum, ordinary Cook's malleable tin metal, five by eight inches long, 22 gauge, made by Westinghouse Electric Company

Technic — Abdominal-Vaginal — 1 The patient is placed upon an ordinary wooden table and draped as for a gynecologic examination. An anterior plate, five by eight inches, is placed over the abdomen just above the symphysis and the same size plate placed posteriorly. Both are connected to one pole of the diathermy apparatus.

- 2 A lubricated concave vaginal electrode is then inserted into the posterior vaginal formix underneath the cervix, the concavity of the electrode facing anteriorly and connected to the other pole of the diathermy apparatus
- 3 The current is then gradually increased so that the maximum amount, 2500 milliamperes, is reached in about ten to 15 minutes and this is maintained throughout the treatment

Abdominal-Sacral—In the abdominal-sacral method, the same size plates are used but the anterior plate is connected to one pole of the diathermy apparatus and the sacral plate to the other pole. The current is raised to 3000 milliamperes.

4 Until patency is established, the patient receives two tubal insufflations a month, each immediately following the diathermy treatment. The pressure is kept at 200 mm of mercury at first for 15 seconds, then 30 seconds, and finally as long as 60 seconds, depending upon

the degree of pain and discomfort it causes. After patency is established the patient receives one tubal insufflation a month, one week after the menstrual period, immediately following the diathermy treatment, until normal tubal contractions are obtained or approximated

The combined treatment of diathermy and tubal insufflation may produce a favorable result in patients in whom the tubes are the seat of extensive strictures, agglutinations, and adhesions which can be overcome by a pressure of approximately 200 mm of mercury.

Success is less likely when the tubes are organically altered as in hydrosal-pinx. There, a pressure of 200 mm of mercury only rarely produces an artificial opening. Although a pressure greater than 200 mm of mercury has opened strictured tubes, without the use of diathermy, the author has not exceeded the maximum of 200 mm of mercury advised by Dr. Rubin

Operative Treatment - The operative treatment of sterility due to tubal obstruction is evaluated by J P Greenhill 16 When the occlusion is at the fimbriated end, simple release of adhesions may suffice to restore the patency of the tube (salpingolysis) quently, however, the distal portion of the tube must be removed or incised, and in one of many ways a permanent opening is made (salpingostomy). When an obstruction exists only in the midportion it is best to remove the site of obstruction together with the distal portion of the tube and perform a salpingostomy on the proximal portion. This is simple: than removing that portion of the tube containing the obstruction and suturing the incised ends in apposition obstruction is in the uterine end of the tube, the operation generally performed consists of the removal of the cornual

part of the tube together with a portion of the uterine corner and implantation of the distal, normal tube into the uterine cavity (tubal implantation) A second way to treat tubal obstruction situated at the cornal end is to remove the entire tube and implant half of the corresponding ovary still attached to its pedicle on the cornua (Estes operation). A third operative procedure to overcome obstruction at the cornua consists of the removal of the tube and implantation of the entire ovary inside the uterine cavity (Tuffier operation)

A review of the literature concerning salpingostomy and tubal implantation for the purpose of overcoming sterility does not present a favorable picture for these operations. The chief reasons for this are the relatively few live babies secured by these measures, the disproportionately high number of ectopic pregnancies which have resulted, and other complications which may follow such operations

An analysis of about 818 plastic operations reported revealed that 54 pregnancies took place after these operations, an incidence of 66 per cent, or one pregnancy for every 15 operations. However, since there were only 36 live babies delivered, the incidence of a successful result was only 44 per cent or one baby for every 22 5 operations. Ten of the 54 pregnancies (185 per cent) ended in abortion and eight (148 per cent) were ectopic pregnancies. Hence only 667 per cent of the 54 pregnancies resulted in live children.

There is certainly much more justification for doing them when the abdomen is opened for some specific indication, such as chronic appendicitis, ectopic pregnancy, or the removal of an ovarian cyst, than there is for performing the laparotomy solely for the purpose of operating on the tubes to correct sterility

VULVA

Pruritus Vulvae

Treatment - This subject was presented by Vayssière¹⁷ at the tenth Gynecologic and Obstetric Congress held in Paris The author states that from eight to ten per cent of all patients who applied for treatment at gynecologic dispensaries desired relief for this condition Among the local causes leukorrheal discharge was the most frequent The pruritus was more marked during menstruation and pregnancy Hormonal factors, such as estrogenic insufficiency, also must be searched for in the etiology Local treatment of the cervico-vaginal infection must be governed by the pH of the secretions, with acetic or lactic acid if they are too alkaline and vice versa A 1 2000 solution of silver nitrate is efficacious A trichomonas infection is best treated by acetarsone. Radiotherapy is to be recommended for cases resisting all other treatment If there is evidence of hormone insufficiency, relatively large doses, from 3000 to 50,000 units a week should be given, of estradiol benzoate in oil, subcutaneously Surgical treatment is a last resort after all nonoperative methods had been unsuccessful Minor methods include local injections of a 1 400 solution of quinine and urea hydrochloride, of 60 to 90 per cent alcohol and of radioactive preparations Presacral nerve resection had given good results in ten of 17 cases, four were partly successful and three were failures This operation is indicated only when every other method has failed to give relief Labhardt of Switzerland stated that pruritus was a symptom in inflammatory disorders of the vulva, in psychoneurosis and in vulvar leukoplakıa, owing as a rule to ovarıan dysfunction The leukoplakias responded to injections of estrogen, if relatively large doses were given

LYMPHOGRANULOMA

Introduction — The term venereal lymphogranuloma is preferred by the Council of the American Medical Association to the numerous other descriptive names that have been applied such as lymphogranuloma inguinale, syphilitic bubo. Durand, Nicolas and Favre disease, climactic bubo, nontuberculous granuloma, granulomatosis lymphatosis and tropical bubo The avoidance of the confusion caused by this unnecessary multiplicity of terms is now especially important in view of the great extension of the disease, which is spread over every quarter of the globe and is found along the coasts of Africa, in the two continents of America and in Asia, as well as ın Australia

Etiology—The disease is probably due to a virus, but the specific agent has not as yet been identified with any great certainty Certain, it is, however, that the disease is truly venereal and is spread by sexual congress. The period of incubation before the appearance of the primary lesions has been estimated, according to D. T. Prehn at from three to seven days. In patients with a positive Frei reaction, the period of incubation was from two to nine days.

Pathology—The pathologic anatomy of the disease is quite characteristic Macroscopically, the extirpated glands consist of conglomerations, with the cut surface in many instance of a red to violet tinge. Abscesses are sometimes observed, even macroscopically. The microscopic examination of the glands discloses the picture of a subacute or subchronic lymphadenitis. Four clinical types are found, namely, an ulcerous type, a nodular form, a papulous form and a specific urethritis. The general symptoms are almost constant and consist of fever, anorexia, emaciation and a feeling

of general weakness. After the adenitis has existed for some time, the temperature is usually subfebrile

Diagnosis—The most valuable diagnostic and differential diagnostic sign is the Frei intracutaneous test, although there is some difference of opinion as to the most satisfactory antigen to use in the test.

In the last three years at the Massachusetts General Hospital and in private practice, E M. Chapman and E P Hayden¹⁸ saw the several manifestations of venereal lymphogranuloma in 30 white persons of all social levels, most of whom have never been outside New England Furthermore, the confusion of this disease with other venereal diseases, malignant tumors, tuberculosis, Hodgkin's disease or simple traumatic infection gave them startling evidence that this disease entity is passing unrecognized in white people These facts predict a wider recognition of a condition that can no longer be regarded as climatic, racial or rare

Venereal lymphogranuloma is venereal in origin, having its onset with a genital lesion that may pass unnoticed, from one to three weeks after exposure. This lesion may be a fleeting herpetic lesion resembling herpes praeputialis, an ulcerative lesion, a nodular lesion or a nongonococcic urethritis, the discharge showing only polymorphonuclear leukocytes without organisms. Nonvenereal and extragenital infections are extremely rare but possible

The 30 patients described had Frei tests positive to human antigen. In the entire group of cases a previous history of gonorrhea was obtained in six and the gonococcus complement fixation test was positive in three. The routine Hinton and Wassermann tests revealed the presence of syphilis in four, only one of these four patients was cognizant of

his disease, and he had received some treatment after it was acquired in 1915.

Treatment-Opinions with regard to therapy are numerous and conflicting. Since the disease has a considerable tendency to spontaneous healing, the results of treatment must be judged conservatively The course of the disease can be shortened considerably by early operative measures aimed at total enucleation of the involved lymph glands. Various tartrates and the intracutaneous administration of graded doses of potent Frei antigen every other day for at least eight doses injected near the site of the lymphadenitis seem to offer the most promising of the nonsurgical treatments In the authors' experience with the acute disease, bed rest, nursing care, local heat applied to the bubo to hasten abscess formation and simple aspiration of the pus are most important in returning the patient as quickly as possible to a useful life He will, however, continue to harbor the disease. At best, the patient can be told that the disease comes on over a period of weeks, is in full bloom for a few weeks and subsides in the course of the following months or more. The most serious effect of this disease, and the most difficult to treat, is the involvement of the lower part of the rectum and of the vulva and perineum Surgical incision and drainage are necessary in late cases with fistulas. An instance may occasionally arise in which the perianal infection 18 50 widespread and intractable that colostomy is indicated

Lymphogranuloma Inguinale

M S Wien and M O Perlstein¹⁹ report a series of 500 patients with *lymphogranuloma inguinale* and call particular attention to ulceration of the skin as part of the genitoanorectal syndrome of this disease which has not received sufficient notice

Diagnosis—The ulcerative lesions oc curring in lymphogranuloma inguinale are superficial in character, irregular in outline and variable in size and contour The normal skin may merge abruptly with the ulcer or form a thin overlapping cordlike band with a tendency to serration The walls of the ulcer are usually of a shallow, shelving type The base of the ulcer is vivid red, shining, and of a smooth velvety texture There is an absence of verrucous nodules or granulations in the base or margins of the ulcer A thin, clear mucoid secretion may cover the lesion In neglected cases this may assume a purulent character The ulcer spreads by peripheral extension, is not auto-inoculable and shows no tendency to spontaneous healing The lesions are painful on palpation The Frei test is positive Histologic examination reveals a nonspecific microscopic picture of tissue suppuration with ulceration of the skin and a predominance of plasma cells in the infiltrate No organisms are seen in the stained sections

Differential Diagnosis — This condition must be differentiated from those entities associated with superficial ulceration of the cutaneous surface Chief among these are chronic chancroidal infection, granuloma inguinale, ulcerative tertiary syphilis, tuberculosis, cutis, gonorrhea, ulcus vulvae acutum (Lipschutz), ulcus vulvae simplex chronicum, traumatic ulcer and epithelioma

(1) Chronic chancroidal infection is a contagious and auto-inoculable ulceration caused by the streptobacillus of Ducrey The lesions are usually multiple, painful, dime-sized (18 mm) ulcerations that have perpendicular undermined edges, a dirty yellow base and a foul smelling discharge The associated inguinal adenitis or bubo is a unilobular lesion which drains a thin foul smelling pus containing the Ducrey bacillus.

dnielcos and Ito-Reinstierna reactions are positive

- (2) Granuloma inguinale is a superficial ulceration of the skin produced by Donovan bodies. The ulcers are contagious and auto-inoculable and present numerous shiny verrucous vegetating nodules of granulation tissue at the margins and dispersed throughout the base of the ulcer This ulceration after healing produces a dense white contracting scar tissue. The process is painless and, as a rule, unaccompanied by adenopathy
- (3) Ulcerative tertiary syphilis results from the coalescence of groups of discrete "punched out" ulcers that tend to assume an arciform or annular configuration and heal spontaneously, producing a thin white atrophic scar with hyperpigmented borders. The serologic reaction of the blood is positive and the condition involutes with antisyphilitic treatment.
- (4) Tuberculosis cutis of the ulcerative or gummatous variety presents irregular painful ulcers and fistulas, the base of which is uneven and covered with yellowish granulation tissue. Smears of the discharge or stained histologic sections reveal the tubercle bacilli. The histologic picture reveals a tuberculous architecture.
- (5) Ulcus vulvae actum (Lipschutz) is a painful recurrent ulceration of the external genitalia. The ulcers are superficial, painful and not auto-inoculable and they heal spontaneously. B. crassus is usually present in the ulcers.
- (6) Ulcus vulvae simplex chronicum occurs in old prostitutes and affects the fourchette. It has not a tendency to spread and is not associated with inguinal adenopathy, hypertrophy of the vulva or stricture of the rectum. The Frei and dimelcos tests are negative.
- (7) Gonorrheal infection may produce a vulvitis associated with erosive lesions, the margins of which may be variable

and the base a dusky red and with a granular surface Smears are positive for gonococci.

- (8) Traumatic ulcers have a characteristic, irregular or fissured form with a preceding history of injury. The lesions heal with marked rapidity
- (9) Epithelioma in the genitocrural region is characterized by the occurrence of a granulomatous new growth in which the ulceration occurs as a secondary phenomenon. The lesion is slow in growing, often with rolled pearly margins, and the nodules are friable and bleed freely. Histologic examination reveals the characteristic changes of a malignant condition

Twelve cases of ulceration of the skin occurring in the authors' series of 500 cases of lymphogranuloma inguinale were observed and are reported with clinical, bacteriologic and histologic records of three cases

Three types of ulceration of the skin are demonstrated by the cases described

- (a) Ulceration of the skin only
- (b) Ulceration of the skin secondary to an existing lymph gland involvement
- (c) Ulceration developing on an esthiomene

The bacteriologic flora of the ulcerations was thoroughly investigated. The organisms found were probably secondary invaders

The authors feel that cases of superficial ulceration in the skin, resistant to the ordinary or specific methods of therapy, especially when occurring in the genitocrural area, should be tested with Frei antigen, diagnostically and therapeutically, in order to rule out the possible relation of the ulceration to lymphogranuloma inguinale

A Haim and C Mathewson, Jr ²⁰ emphasize the public health importance of this disease due to its frequency in the white population. These investigators

have collected 46 proved cases in northern California. The importance of the Frei test in diagnosis is stressed. The Frei test plays the most important rôle in the diagnosis of lymphogranuloma inguinale. From one of their patients they were able to collect sufficient pus for the preparation of a satisfactory antigen, which they have used consistently since April, 1936 Other antigens have been prepared from later cases The pus was secured by aspiration from unbroken fluctuant buboes If it proved to be bacteriologically sterile, it was diluted 1 6 in sterile saline solution and the virus killed by heating the diluted pus to 140° F (60 $^{\circ}$ C) for two hours on one hour on the following day Antigens so prepared provide excellent mediums for the multiplication of bacteria, consequently the greatest care must be exercised in its use to prevent contamination

Any antigen must be tested for its specificity and potency in proved cases and in a sufficient number of controls. Whether or not small amounts of blood contained in the pus removed will interfere with the specificity of the antigen will become evident from these tests. If properly kept in an icebox, antigens remain effective for a period of from one to two years. It is necessary, of course, to check the specificity and sterility of the antigen from time to time.

Frei Test—In performing the test, 0.1 cc of the antigen is injected intracutaneously, preferably on the flexor surface of the forearm. The positive reaction is a delayed one. A red papule appears about 24 hours after injection and increases in size up to 48 or even 72 hours. The authors usually do the final reading after 48 hours, noting the diameter in millimeters of the red papule and of the surrounding erythematous halo, if present. They consider the reaction positive if the diameter of the papule

was 6 mm or more Reactions smaller than this, or different in character and yet suggestive, have been designated as questionable. As in other tests, especially the Wassemann reaction. Questionable reactions must be checked and interpreted on the basis of available clinical and historical data.

The positive test gives evidence of an acquired specific allergy, which in most instances continues throughout the life of the patient. Consequently a positive test does not necessarily indicate the presence of a recently acquired active infection. Old completely healed infections may eventually give positive reactions. Negative reactions may be seen in cases in which the specific allergy has not yet developed or in those in which the reaction is suppressed by factors known to lower the allergy in other infections. It is stated the *syphilis* may prevent a positive reaction to the Frei antigen.

VAGINAL TRICHOMONAS

The possibility of auto-infestation is an important factor in the prevention and treatment of trichomonas vaginitis P B. Bland and A E Rakoff²¹ discuss the incidence of trichomonads in the vagina of 200 women

Distinct differences in morphologic characteristics among the three forms have been demonstrated by the careful comparative studies of Wenrich, and more recently by the investigations of Powell It has been suggested by Andrews, Lynch, Dobell and many others that under similar environmental conditions the species may be identical, apparent distinctions being the result of differences in habitat Experimental animal inoculations have been advanced by Hegner and by Dobell in support of this contention while the experiments of Kessel and Gafford and of Bonestell indicate

an organ specificity for the trichomonads of human hosts

On the basis of inoculations into human hosts Karnaky believes that infestation of the vagina may be produced with trichomonads of intestinal and buccal origin and states that these "convert into the vaginal form when transplanted into a trichomonal free vagina" although no criteria or discussion of observations are given to substantiate this statement. We have not been able to confirm Karnaky's results with the intestinal and buccal forms, although we have been able to produce a vaginal infestation with trichomonas vaginalis from culture

From a clinical point of view, trichomonas vaginalis is the most common as well as the most important cause of human infestation by trichomonads, since the leukorrhea and vaginitis with which it is so frequently associated are generally acknowledged to be caused by the flagellate. The opinion has frequently been expressed by clinicians that vaginal infestation has its origin from intestinal or buccal contamination.

The belief has led to the institution of improved hygienic measures, especially with a view to preventing vaginal infestations after initial local treatment. However the practice of giving drugs by mouth, as suggested by Bradley and Karnaky, or of adjusting gastric acidity, as reported by Bogess, not only has little scientific justification but, when such drugs as arsenicals are given, may be actually dangerous to the patient's health, in addition to removing emphasis from rigorous local treatment. At the very least, examination for intestinal trichomonads, should be made before the treatment of a condition which may not exist is undertaken

It has been demonstrated in the present study that where vaginal trichomoniasis is common, intestinal infestation

with trichomonas is rare and even when present is not more frequently associated with vaginal infestation than would be expected from chance distribution The latter fact is of especial interest because it has been demonstrated that, among the patients harboring trichomonas hominus, the organisms may be repeatedly demonstrated in the feces over a considerable period of time, thus affording ample opportunity for vaginal infestation to occur In a study of a large number of oriental women Matsuda also noted that there was no tendency for the patient to be parasitized with intestinal and vaginal trichomonads at the same time. The incidence of intestinal infestation among the 200 patients in the present study is in general agreement with those noted for other groups in this climate Craig estimates that in temperate regions from 05 to 1 per cent of individuals examined harbor trichomonas hominis Hegner and Payne, from a review of 35 papers by American, English and French investigators including 20,000 cases, estimate the incidence at three per cent Lynch believes the percentage in warmer climates and in patients with gastrointestinal disturbances is considerably higher

Vaginal auto-infestation with buccal trichomonads has received considerably less attention than has infestation with the intestinal form, although his possibility has been emphasized by Lynch On this assumption the much higher incidence of the buccal trichomonads as demonstrated in this study, as well as by Beatman, Hinshaw, Hogue and others, together with the fact that saliva is commonly used in sexual practices, would indicate that this is a considerably more prevalent source infestation than would be possible from fecal contamination Further, it has been pointed out by Bland, Wenrich and Goldstein that mor-

phologically Trichomonas vaginalis more closely resembles the buccal form.

From the data of the present study auto-infestation from the buccal source was considered improbable for the following reasons (a) the comparatively low incidence of buccal trichomonads, (b) their scant numbers even in positive cases and (c) the failure to note any considerable increase in incidence in vaginally infested patients

It has been generally accepted that cysts or other resistant stages of trichomonas do not exist and consequently that intestinal infestation requires the successful ingestion and gastric passage of the motile forms. This mode of intestinal infestation has been demonstrated by animal inoculation by Hegner and by Wenrich and Yanoff. If successful transference of trichomonas from one source to another is possible, an incidence of intestinal infestation many times lower than buccal trichomoniasis in the same group of patients, as obtained in this study, remains to be explained.

Vaginal infestation with trichomonas was common, occurring in 23.5 per cent of the group. Buccal infestation occurred in 16.5 per cent of the patients while intestinal trichomomasis was comparatively rare, being present in only 1.5 per cent of the women.

It was demonstrated that the wet smear method is the most efficient for the diagnosis of trichomonas vaginalis while the culture method was much superior for the detection of the intestinal and buccal trichomonads

Women harboring vaginal trichomonads did not show an appreciably higher percentage of buccal or intestinal trichomonads than was noted for the group at large. Only one woman (0.5 percent) harbored all three organisms

Rectal contamination was regarded as an improbable source of vaginal infes-

tation in view of the rarity of intestinal trichomoniasis among women with trichomonas vaginitis.

Of three patients harboring intestinal trichomonads, only one was positive for trichomonas vaginalis despite the fact that the flagellates could be regularly demonstrated in the feces over long periods of time

Autoinfestation with buccal trichomonads was also considered an unlikely source of vaginal infestation because the dual incidence of these organisms was not more than would be expected from chance distribution

A comparison of the incidence of trichomonads from the bowel and mouth indicates that intestinal infestation probably does not result from ingestion of the buccal forms

Trichomonas Vaginitis

The use of *silver picrate* in treatment is advocated by R von L Buxton and H A Shelanski ²² Their method of treatment is as follows

After a positive diagnosis of trichomonas vaginitis had been made, the patient was placed in the lithotomy position and 5 gm of silver picrate-kaolin powder was blown into the vagina by means of a special insufflator, care being taken to use only enough pressure to balloon out the vaginal walls. The patient was then given six vaginal suppositories of silver picrate, one to be used each night, and she was instructed to return in one week. At this time a sinear was taken and the vagina again was insufflated with silver picrate-kaolin powder and six more suppositories were supplied The patients were examined for trichomonas seven and 14 days after the original insufflation, and also at the end of each menstrual period for the next six to nine months Cultures of the

vaginal secretion for trichomonas vaginalis were made at each examination.

Of the 168 patients found to harbor trichomonas vaginalis, it was possible to treat and follow up 100 individuals, 62 for six months and 38 for nine months There were three recurrences in this group, occurring at the fifteenth, eighteenth, and twenty-first week after the original treatment in three patients Two of these were again treated and remained negative up to their last appearance at the clinic, at the seventeenth and twenty-second week following the second course of treatment At the end of the two-week period of treatment, it was found that the discharge disappeared in 90 per cent, the itching in 94 per cent, and the burning in 96 per cent of the 100 patients, and smears and cultures were negative in 100 per cent

The authors conclude that the use of one per cent silver picrate-kaolin powder in combination with silver picrate suppositories is an efficient and simple method of treatment of trichomonas vaginalis vaginitis

Trichomonas Vaginalis

H C Hesseltine²³ discusses the therapy of vaginal trichomoniasis. He studied the therapeutic effect of three arsenical, one silver picrate and two lactose preparations. A special search for foci of infection was undertaken when patients did not respond to the therapeutic agent in question.

The author observed that good results may be obtained with various agents in approximately 85 to 90 per cent of the patients, while the remaining 10 to 15 per cent may not remain relieved or may even fail to be improved Even though many husbands whose wives were in the unimproved groups refused urologic examinations, three of those exam-

med were found to have prostatic infections.

The majority of patients with vaginal trichomoniasis can be benefited by more than one therapeutic material and method

Probably in from 8 to 15 per cent of the cases of vaginal trichomoniasis particular care should be taken to eliminate foci of infection from the patient's rectum or urethra and bladder, or from the husband's urethra and prostate and perhaps from other sources still undetermined

The physiologic restoration of the vagina is apparently of paramount importance in accomplishing cures

The author concludes that an adequate and proper control should be employed in the evaluation of the merits of any procedure or preparation

A E Rakoff, in discussion of this paper states that to his experience only ten per cent of a group treated by kaolin insufflations alone responded permanently, although almost all were temporarily relieved. It is notable that the drugs employed were all in a dry form It is the present consensus that "dry antisepsis" affords the most successful basis for elimination of the flagellates Two preparations were insoluble pentavalent arsenicals, acetarsone and carbarsone P B Bland and Rakoff made a study of these drugs plus a related soluble derivative, sodium-methylene-sulfonamino-hydroxy-phenyl-arsonate. The latter was more effective clinically and in vitro The realization that organisms are harbored in surrounding structures may mean the difference between cure and recurrence The urethra and paraurethral structures are the most common offenders, since trichomonads are frequently found here A few organisms harbored in the cervix may also be the source of recurrence

The male is probably a source of reinfestation in a small group of cases He found the organisms in about six per cent of a group of men The anterior urethra was much more commonly the seat of infestation than was the prostate gland The intestinal tract is rarely if ever the source of vaginal infestation Evidence indicates that the vaginal and intestinal trichomonads are morphologically and culturally distinct and that in this climate intestinal infestation is relatively uncommon Experimental inoculations with the intestinal forms were unsuccessful, whereas he has produced the infestation with vaginal trichomonads Administration of toxic drugs by mouth or bowel to eliminate an intestinal infestation whose existence is not first proved is hardly justifiable, yet many patients are treated in this fashion Exanimation of the vaginal bacteria affords a reliable indication of progress during the course of treatment Doderlein's bacilli tend to become re-established with the disappearance of the trichomonads Lactose or lactic acid douches are sometimes helpful in favoring this return after preliminary chemotherapy

Vaginal Moniliasis

Experimental Data — Infections of the vagina and vulva with monilia form the basis of an experimental study by P R Bland, A E Rakoff and I J Pincus ²⁴

Vulvovaginitis was produced in 29 of 50 women, 38 pregnant and 12 nonpregnant, inoculated with pure cultures of monilia of vaginal origin

By inoculation of similar groups of 12 pregnant and 12 nonpregnant women with the same strains of monilia it was demonstrated that pregnancy is a predisposing cause of monilial vulvovaginitis

The increase of the glycogen content of the vaginal mucosa which occurs during pregnancy is regarded as the fundamental factor in producing a favorable medium for the growth of monilia in the vagina of the pregnant woman.

White women appeared to be somewhat more susceptible to infection than negro hosts.

Variations in age within the childbearing period did not influence the percentage of successful inoculations

Primigravidas were more susceptible to infection than multigravidas.

The stage of gestation, from the third lunar month of pregnancy to erm, bore no relationship to the number of successful inoculations

Leukorrhea due to various causes was an inhibiting factor in the production of vaginal moniliasis

The incubation period varied from 24 to 96 hours. The average period of incubation was 39 hours.

Thrush involvement of neighboring cutaneous surfaces occurred in five of the 50 women inoculated with vaginal monilias. The cutaneous lesions appeared only in the patients with severe vaginal infections remaining untreated for six or more days and consisted of hypertrophic marginated papules covered with a soggy white scale, together with pinpoint vesicles and pustules

Successful inoculations resulted from the introduction of monilias isolated from patients without signs or symptoms of moniliasis as well as from that of organisms obtained from patients with severe infections. A higher percentage of infections, however, was obtained with monilias from the more virulent infections.

Inoculation into the vaginae of 12 pregnant women of three strains of monilia isolated from typical lesions of oral thrush produced moniliasis in seven

instances Cutaneous involvement was noted in one instance. It is concluded that the organisms of vaginal moniliasis and those of oral thrush are of a similar degree of pathogenicity.

Gonorrheal Vaginitis

Treatment—The treatment of vaginitis of children and of women after the menopause is summarized by R M Lewis and E L Adler ²⁵ The authors report 82 cases of gonorrheal vaginitis in children treated only with amniotin (estrogenic) suppositories in the Children's Medical Service of Bellevue Hospital, New York, plus the recent results of other clinics furnished them

To be specific, this form of treatment consists in the insertion of a gelatin capsule containing 75 rat units of amniotin, or one-half of an animotin suppository, into the vagina each night at bedtime (One-half of a suppository contains 1,000 international units of estrogenic substance) No douches are used, but at first the external genitalia may require cleansing if the discharge is profuse

At the Bellevue Hospital they found that in 107 courses of such treatments the vaginal smears became negative (absence of pus and gonococei) on an average in 24 days. A few patients required many weeks before negative smears were obtained, on the other hand some cleared up in a very few days. Satisfactory results require faithful daily treatment. Some of their patients required unduly long treatments because this fact was overlooked.

Of a total of 82 patients with gonorrheal vaginitis adequately treated with ammiotin suppositories alone in the Children's Medical Service at Bellevue to April 15, 1937, two were not cured The remaining 80 are apparently well Twenty-nine have been cured for over one year, 21 for over six months and the other 30 have been apparently well (negative smears, and the like) for from one to six months. One of the two uncured cases was puzzling because there no physiologic response even after the administration of large amounts of substance

Together with others now using this method of treatment they found that reinfections and recurrences were a serious problem Twenty-five of our 80 patients returned from their homes again with vaginitis after having been apparently cured They believe that most of these cases were reinfectious. In the homes of 12 of these children there were other persons with gonorrhea It seems probable that these patients reacquired infections from their original sources One case recurred while the patient was in the hospital, but this was also a reinfection These patients, when they returned, were cured by being treated as before with suppositories It is of interest that patients treated a second time usually get well more quickly than do patients having their initial treatments They believe that all patients should be under observation for at least one year after they are apparently cured. They should be kept from intimate contact with other girls for at least the first six months of this time. It seems unnecessary to add that, if the treatment with suppositories is unsuccessful, a careful investigation of the cervix, urethra and rectum must be made They have found but few instances of persistent endocervical infection

R A Benson, and Arthur Steer²⁶ have reported the hypodermic treatment of 80 patients with different preparations of estrogenic substance Sixty-six were apparently "cured" but in nearly all the condition recurred In a later group of 92 cases Benson used amniotin capsules

Intravaginally for an average of 21 days Negative smears and apparent cures were obtained, but after the patient returned to their homes about one half were reinfected or the condition recurred. He observes that "an analysis of these cases would seem to indicate in general that those showing recurrence were the ones returned to unclean homes, while those that remained cured went back to clean homes or child caring institutions where there was no contact with infected cases" Benson believes also that apparent recurrences after discharge from the hospital are usually reinfections

The cost of the suppositories of estrogenic substance used in the average case is not excessive for the private patient (amounting as a rule to eight or ten dollars). Since only relatively small amounts of estrogenic substance are given by suppositories, it is our opinion that the treatment is not dangerous. No ill effects have been seen. However, the authors advise against the administration of large doses of estrogenic substance over a long period of time as possibly injurious, although there is no conclusive evidence of harmful results following such treatments.

Until recently the treatment of semile or postmenopausal vaginitis has been most unsatisfactory. After cessation of the secretion of estrogen following the menopause or castration, the vaginal mucosa reverts to the thin, ill-developed structure of childhood. The secretions are no longer acid and the mucosa becomes once again easily infected. When infected, such patients complain of burning, itching or pain in the vagina, and coitus may be painful or impossible Remarkable success is reported in treating these cases with amniotin subcutaneously. In the majority of his cases 100 rat units of amniotin are given hypodermically three times a week The average duration of the treatments is six weeks Vaginal suppositories alone do not give satisfactory results Usually complete symptomatic relief is afforded in about ten days. Biopsies taken at intervals during treatment show the development of the vaginal mucosa in appearance exactly similar to that of a woman during the years of menstrual life The vaginal secretions also become acid. The treatment of such patients should be continued for from six to eight weeks, for if any infection of inflammation remains the symptoms will return soon after it is stopped In any event, when treatment is stopped the vaginal mucosa reverts to that of the childhood type, and if the factors that were responsible for the original infection are again encountered reinfection will follow

Results have been good when the condition treated was a typical senile vaginitis. Vulvar leukoplakia has not been benefited. The authors have had two cases, one after removal of the ovaries and one following intrauterine irradiation, in which the shrunken vagina became so dry and sensitive that intercourse was impossible. In both instances treatment with ammiotin was effective in relieving the situation.

Gonorrhea

Treatment—The treatment of gonorrhea in the female by a combined heating technic is described by W. Bierman and E. A. Horowitz ²⁷

They have used this method during the past six years in 721 cases with success in 113 (93 per cent). The treatment is strenuous, and not without danger. It is a hospital procedure. Adequate apparatus, trained personnel, and continuous watchfulness are necessary. Physically induced fever is combined.

for six hours with *pelvic diathermy*, and for two hours with *pelvic short wave*, so as to produce a vaginal temperature of about 109° to 110° F (428° to 433° C), while the body temperature is held between 1055° and 1065° F (40.8° and 414° C) and continued for a period of about 12 hours. While usually one to three such treatments may be required to eradicate all gonococci, the average number found to be necessary in our last series was 14 per patient.

The outlook for the woman with gonorrhea has been brightened by the development of the combined heating procedure here described A rapid eradication of the gonococci can be achieved in most cases, and without danger of extension of the disease. The possible dangers of the heat treatment itself require that it be administered in hospitals, and only by those sufficiently qualified by special training and experience

Cervix - Inflammation

Treatment—J R Goodall and R M H Power²⁸ discuss the treatment of inflammatory disease of the cervix They divide this subject into

- 1 Vonsurgical treatment
- 2 Surgical treatment
- 3 The influence of a residual inflammatory cervical disease upon pelvic operation
- 1 Nonsurgical Treatment There are very few forms of treatment of the inflamed cervix that offer any hope of recovery or even amelioration other than the thermocautery. Prior to its introduction, the medical profession leaned strongly to preparations of fincture of rodine, carbolic acid and other escharotics. Later, diathermia and "Elliot" enjoyed a vogue. These have been abandoned for the more rapid, more controllable and more effective electric thermocautery.

Thermocautery is a very effective form of treatment when properly applied in suitable cases, especially if one does not wish to destroy cervical function An excellent result can be anticipated only in those cases that are mild, and limited chiefly to the surface epithelium lining the cervical canal: chronic catarrhal endocervicitis It is most effective in nulliparas, and in early treatment after each delivery. It becomes progressively less effective the more widespread the disease, the deeper it has involved the cervical stroma, and the greater the organic departure of the cervix, as a whole, from its normal size and consistence

In nulliparas, one should be careful not to cauterize the external os overvigorously where there is no ectropion Where, on the other hand, there is ectropion, there is no such risk because the larger the area of ectropion, the more will the external os be patulous and soft In cauterizing the canal it is not necessary to cleanse the canal of mucus with caroid or other solvent In fact, fluid in the canal is a great advantage, for, when it boils, it distributes the heat equally and generally over all the interstices of the canal, so that there is no necessity of bringing the cautery point into contact with the canal epithelium at all When the canal presents a whitish or parboiled appearance, the treatment has progressed far enough Treatment so effected will not produce a pocketed and tortuous cervical canal, because the heat is evenly distributed. Frequently, in the next ten days, a thin cast of the canal is shed or the necrotic tissue is disintegrated, leaving a pink healthy mucosa. The objects of the cauterization are not only to destroy the diseased cervical mucosa, which is the seat of irritative hyperfunction or hyperplasia, but also to destroy the subjacent hyperanemia and hypervascularity, which can

be done effectively only by a dull penetrating heat A white heat will not only just scar the surface, but will destroy the platinum points The knife should move slowly over the surface and should penetrate only about 1/16 of an inch, but slowly enough to coagulate the supernumerary subjacent blood vessels When larger, discrete vessels emerge from, and course over, the area toward the periphe-y, these should be destroyed with a finer cautery point, at their point of egress Similarly nabothian cysts should be punctured and the contents caused to boil with prolonged contact Sterile paraffin is then applied to the cervix and vagina Douches are not begun until 24 hours after cautery

Cauterization of the cervix should be done as soon as convenient after cessation of a menstrual period. By choosing this time there will be less bleeding, better healing, and less disturbance of the succeeding menstrual phases. If treatment is instituted after the middle of the intermenstrual period, the subsequent menstruation may be greatly advanced, together with an increase in duration and quantity.

Cautery of the cervix is contraindicated in gonorrheal disease except where it is confined to the cervix, a rare condition and a very difficult one to determine

The authors emphasize the harmful results, that may follow deep cautery of the cervical canal with a large cautery or cautery kinife, extending from ½ to ½ inch in depth, in the hope of reducing a large hard cystic cervix. In the first place, pathology shows the futility of this procedure, and in the second place, it so cicatrizes the cervix that dilatation at subsequent labors may be greatly inhibited or impossible. There is no cure for such a large fibrous cervix. Its bulk

will greatly reduce after menopause, natural or artificial

2 Surgical Treatment—It is almost impossible to remove all the diseased mucosa by the deepest coning out during amputation Drainage is frequently blocked and healing is frequently only by secondary intention. Amputation of the cervix for the cure of endocervical disease is being discarded in the larger clinics, but is still all too frequent in the smaller centers and hospital.

Two complications frequently follow upon the cervical operations in the presence of endocervicitis. These are (1) late septic hemorrhage and (2) lack of primary union. The authors denounce cervical amputations and cervical repairs in the presence of chronic mucosal disease.

Pelvic Inflammation

Effect on Upper Urinary Tract-H L Kretschmer and A E Kanter²⁹ discuss the effects of gynecologic lesions on the upper urmary tract During pregnancy and the puerperium dilatation of the ureters and kidney pelves occurring in 100 per cent of their cases There was a return to normal in 593 per cent after two weeks and in 343 per cent after six weeks, and the remaining 62 per cent were normal after 12 weeks The striking fact about the dilatation of the ureter during pregnancy is that with rare exceptions, it is above the brim of the pelvis Lateral displacement, when found early in pregnancy, tends to increase as the pregnancy advances

In the selection of cases for this study the authors used patients who had no urinary symptoms and who were normal on urinary examination so that they might demonstrate how frequently changes are found in this so-called silent or asymptomatic group. In cases in which there were urinary symptoms, attention is naturally directed toward the urinary

tract, hence changes, when present, are readily found. However, if a group of patients have no urinary symptoms, changes in the upper urinary tract, when present, may be readily overlooked.

Intravenous pyelography was carried out as a routine, using diodrast in 20 cc and 30 cc. ampules This was supplemented by retrograde pyelograms in a few instances in which the intravenous method was not satisfactory or in which they wished to check the results of the intravenous pyelograms

The largest percentage of changes in the upper urinary tract was found in the cases of ovarian cyst; out of a total number of eleven cases, changes in the pveloureterograms were noted in nine cases, or 818 per cent It would appear reasonable to assume that the high incidence of changes in the upper urinary tract in ovarian cysts is probably due to the fact that the cysts, being of soft consistency, readily mold themselves into the pelvis, which results in pressure on the ureters, as seems to be the case in pregnancy If the two very high-lying intra-abdominal ovarian cysts are excluded which, because of their position, could not possibly have compressed the ureter, it is found that the ovarian cysts produce changes in the upper urinary tract in 100 per cent of the cases Therefore it would be reasonable to assume that the consistency of the tumor and its ability to mould or compress has something to do with the high incidence of the changes in the upper urinary tract

In the large fibroids above the brim of the pelvis, 709 per cent showed changes in the ureteropyelograms. When the lateral displacement of the ureter was bilateral, the uterine enlargement was mainly in the midline.

Of the large fibroids above the brim of the pelvis in which there was no dilatation of the upper urinary tract,

it was found at operation that the fibroid growing out of the pelvis left a free interval between the tumor and the brim of the pelvis, so that there was no pressure on the brim of the pelvis In the cases in which there was dilatation, it was found at operation that the fibroid so molded the pelvis that it probably compressed the ureter with resulting dilatation In one case the dilatation was limited to some of the cahces and rapidly disappeared after operation Therefore it is reasonable to assume that pressure seemed to play a rule in dilatation because the dilatation disappeared after the fibroid was removed

It would appear that the incidence of secondary changes in the upper urinary tract in association with various types of gynecologic disorders is high. In this series of 51 cases, evidence of changes in the upper urinary tract was found in 647 per cent. In the group of fibroids, changes were found in 657 per cent, in ovarian cysts, 819 per cent; in prolapses, 25 per cent, in the one case of tubo-ovarian abscess, there was no change in the upper urinary tract

Failure to appreciate the frequency with which these lesions occur is due to the fact that there has been no routine preoperative study in the group of cases that do not present urinary symptoms and urinary signs

Following appropriate surgical procedure, a return to normal takes place in 72 5 per cent

Subsequent pyelograms according to the authors should be carried out in all cases in which recovery has not occurred at the time the patient is discharged from the hospital

Uterine Myoma

Treatment—Fibroids of the uterus which occupy unusual positions and their

surgical treatment are discussed by V. S Counseller 30

Some of the fundamental points to keep in mind in undertaking treatment of myomas are their blood supply, their cleavage planes and their manner of growth Generally speaking, myomas of all sizes are practically devoid of blood vessels They obtain their blood supply from a thin capillary network from the vessels of the myometrium For this reason, operation can be undertaken with practically no fear of troublesome hemorrhage However, this rule does not hold for large pedunculated tumors that have a large pedicle, for the pedicle is usually extremely vascular and large tumors may be soft and filled with excessive amounts of blood, so that retrograde bleeding from the tumor may be severe When this condition is encountered, much blood, which is valuable to those who are anemic as a result of repeated hemorrhages, may be put back into the circulation immediately by injecting from 1 to 2 cc of solution of posterior pituitary into the tumor before its pedicle is clamped. The author has encountered myomas in which the pulsations could actually be palpated in the pedicle of the tumor

Tumors that are growing in the myometrum compress the musculature of the uterus around the utmor and have the appearance of being encapsulated The tumor, which is much firmer than the invometrium, can be readily enucleated when the cleavage plane between the tumor and the myometrium is entered. This is best accomplished by holding the tumor firmly with one hand and incising through the myometrium directly down to the tumor The tumor then 13 visible and the plane of cleavage can be readily entered The capillary blood vessels of the capsule can be best controlled by pressure until the defect in the myometrium is closed by a continuous mattress suture. The line of cleavage in myomas clearly distinguishes them from the adenomyomas, since the latter are intimately fused with musculature of the uterus.

The situation of the myoma in relation to the uterus is highly important in selecting the type of surgical treat-Those which happen to grow from the lower portion of the uterus mav extend laterally into the broad ligaments. under the bladder or posteriorly behind the peritoneum of the cul-de-sac of Douglas In the cellular tissues of the broad ligament the tumor may grow without interruption, it may retain its connection to the uterus or it may become completely separated from the uterus It is frequently in connection with the removal of an interligamentous myoma that the ureter is injured. The veins often are enlarged from pressure and under tension resemble a ureter when it is free from blood. There is one maneuver which, if carried out at this point, will definitely determine whether one is handling the ureter or not. If the ureter is snipped or otherwise irritated with the thumb forceps, it forcibly contracts, this distinguishes it from blood vessels Invattempt to remove a large myoma in this situation, without adequate exposure and without opening the broad ligament wide so that important structures can be readily seen, will result in troublesome hemorrhage and perhaps injury to the ureter and bladder The author always opens the broad ligament posteriorly and then identifies and retracts the ureter at once so that any troublesome hemorrhage can be immediately controlled without fear of injury to the ureter

A myoma that extends from the posterior wall of the uterus far down behind the peritoneum of the *cul-de-sac* of Douglas is one that presents several technical

difficulties in its removal Again the ureters are both pushed laterally, and the tumor grows upward in the mesentery of the sigmoid colon and the cecum. It is usually this type of myoma that is occasionally exposed and considered inoperable, the patient is then subjected to radium or roentgen therapy. If exposure is adequate and the condition thoroughly recognized, the tumor can be removed by careful dissection after retraction of the blood vessels in the fat of the mesentery of the colon The safest method is to begin the removal by cutting through the peritoneum near the point of origin of the tumor and working laterally, always keeping in intimate contact with the wall of the tumor

A myoma that originates from the anterior uterine wall, near the cervix, may cause considerable distortion of the bladder. If in separating the bladder the wall of this organ is injured, it is a much safer procedure to resect the wall of the bladder, leave it attached to the myoma, and then close the bladder with two rows of number one plain catgut sutures

Myomas that grow toward the uterme cavity form a distinct group and then surgical management is therefore different. In cases in which the patients are less than 40 years of age, these myomas should be removed surgically Two methods are available. First, if the cervix is thoroughly dilated the tumor may be grasped with a tenaculum, and then with one hand on the fundus to hold it in position the tumor may be extracted from the uterme wall by careful rotation and gentle traction. Subsequent bleeding is rarely of major importance and is usually controlled by packing the uterus with gauze for from 24 to 48 hours. Second, if this maneuver is unsuccessful, the myoma should be removed by abdominal myomectomy and always by the latter procedure if there are other myomas in the myometrium or subserous myomas, which also should be removed

Pedunculated submucous myomas behave exactly as does a foreign body in the uterine cavity. As the tumor increases in size the uterus endeavors to expel it, the same as it does a large blood clog Vaginal myomectomy is the only procedure ever to be employed in the removal of such myomas patient is a woman who has been pregnant, adequate exposure is always possible, but if she is a nullipara it may be necessary to secure exposure by deep lateral episiotomy. The tumor should be grasped with the hand and not with instruments, for such tumors are soft, friable and hemorrhagic The tumor may be gently pulled downward and the The cervix is often pedicle inspected large and soft enough to permit one to examine the interior of the uterine cavity by inserting the index finger along the The only other point which must be noted in the complete removal of such tumors is the union of the pedicle with the uterine wall Should this be disregarded, an effort to remove all the pedicle may inadvertently result in an opening through the uterine fundus, which is also very soft. The point of attachment can usually be detected with good exposure and direct light rarely necessary to ligate or suture the stump of the pedicle to control bleeding

Cervical involves, which fortunately are not common, present one of the most difficult surgical situations in gynecology. Their removal is necessary and always difficult on account of their position and the inherent danger of injuring adjacent structures. These tumors, according to Robert Mayer, are unlike the fundal involves in that they are not influenced by the sex hormones and therefore do not undergo regression after the menopause. When excessive hemorrhages de-

velop they are often treated by roentgen rays, on account of the technical difficulties presented in their surgical removal, which as a rule is inadequate Unlike the pedunculated myomas, which protrude through the cervix, they are not infected, therefore, surgical exploration can be instituted immediately On account of their tendency to grow backward toward the cul-de-sac of Douglas and upward, the abdominal type of hysterectomy is preferable. Although myomectomy is possible if the fundus of the uterus is not involved by the myoma it will occupy a position on top of the tumor and usually will be situated near the umbilicus The ureters, bladder and rectosigmoid must be carefully mobilized during the removal of the uterus

Abdominal myomectomy, subtotal hysterectomy and total hysterectomy may also be considered in the treatment of myomas. The choice of any of these procedures depends on the size, number and situation of the tumors, on the age of the patient and on the condition of the cervix. Myomectomy, which must always be given consideration in cases in which removal of the tumors is indicated, is one of the most satisfactory operations However, it is more difin gynecology ficult to perform than subtotal hysterectomy, since the technic of the former is necessarily varied to suit the condition Bleeding need not deter encountered the surgeon, as it can be adequately controlled if an assistant maintains gentle traction on the fundus of the uterus during the operation

The question of whether a subtotal or total hysterectomy should be performed when removal of the uterus is indicated for benign conditions should be determined by the condition of the cervix of the uterus. There is no more logic in leaving an infected, lacerated and eroded cervix when the uterine

corpus is removed than there is to fail to extract an infected dental root which is a constant source of septic absorption into the general system

In conclusion the author points out that, since operations on the uterus occasioned by myomas are among the most frequent gynecologic procedures, each patient must be carefully studied and the method of procedure determined by the position of the myoma, whether the tumors are single or multiple, and by the age of the patient

GENITAL MALIGNANCY

Cervix — Carcinoma

Diagnosis — The early diagnosis of cervical carcinoma is emphasized by W Schiller ³¹ The early carcinoma and the small one are not identical. If carcinoma grew very rapidly from its onset, then a small cancer would be a young one, but that is not true. This fact that carcinoma grows so very slowly at the beginning offers a marvelous chance for early diagnosis.

In a monograph which Kermauner published with Schottlander on carcmoma of the cervix, he discussed the important question of how the normal epithelium and carcinoma meet one another in advanced cases. In 95 per cent of cases it is found that between the normal epithelium and the carcinoma a zone exists, occupied by neither carcinoma nor by normal epithelium This zone Kermauner proposed to call the neutral zone or the zone of demarcation In the remaining five per cent of the cases there is instead a small intermediate strip between normal epithelium and carcinoma which is characterized by two points Under the low power it is seen that the height of this epithelium is exactly the same as that of surface epithelium, but with the high power it is clear that the cellular type is exactly the same as the cells found in carcinoma. How should we classify this strip? Should we say it is normal epithelium or should we say it is carcinoma?

The first step toward an earlier clinical diagnosis was to get a clear idea of the histologic character of early carcinoma. The next question was, how to make surface carcinoma visible to the gynecologists Schiller found that carcinoma of the cervix can be differentiated from normal epithelium in about a fifth of the cases by three characteristics. First, this zone is a little elevated Second, the surface is not perfectly smooth and is some-Third, while the normal what dull epithelium of the cervix is more or less translucent, so that the entire connective tissue with arteries, veins, and capillaries shines through and has a slightly violet or reddish tinge, the carcinomatous epithelium is opaque and whitish in color If you describe this early carcinoma you describe it as a white patch or as a leukoplakia About 30 per cent of all cases of beginning carcinoma gave the appearance of leukoplakia

Leukoplakia means "white patch" It is not a pathologic entity, but simply a description, a sign, and means no more than if you say fever or jaundice or edema. These are symptoms but not pathologic entities. Similarly, we should not use leuoplakia in the sense of a clinical diagnosis. The relation between leukoplakia is simply that some of the young carcinomas look like leukoplakias.

What is to be done with the remaining 70 per cent of very early carcinomas that are not visible. Attempts to differentiate these carcinomas with a vital stain were unsuccessful, because it was not possible to find a dye that would stain carcinoma and not stain normal epithelium or vice versa. How the surface layers of normal

epithelium were composed of cells which appear empty when hematoxylin eosin stained, but with a special stain can be shown to be filled with glycogen. This glycogen is not analogous to be glycogen of the liver or of muscle, which is soluble in water. The glycogen of the cervix epithelium is not soluble in water, and consequently we can put the slides in water without losing part of the staining glycogen. These glycogen-filled cells are not found in carcinoma, which gives the basis for a differential test.

The method of staining glycogen is to bring it in contact with iodine Glycogen attracts and stores iodine, and stains a deep brown. We cannot use an alcoholic solution because in that way we produce a surface necrosis, and must depend on an aqueous solution. The best solution is the so-called 1-2-3 solution, which means pure iodine 1 Gm., potassium iodide 2 Gm, and water 300 cc. We can transform a latent carcinoma into a visible carcinoma by using this solution, the surrounding epithelium staining brown and the carcinoma remaining perfectly white

The iodine test serves only to discover a carcinomatous zone in a layer of normal epithelium. This test is of no value, for example, in distinguishing between ulcerating carcinoma and erosion. The differential diagnosis between these conditions has to be made by means of a biopsy.

The incidence of carcinoma is sometimes very high and sometimes very low. The man who examines systematically all cases has a low incidence. The statistics of our dispensary show that in 100 cases there are perhaps 25 with more or less well-developed white spots. Of these 25, one can rule out ten or 15 as being of the hyperkeratotic or traumatic type. Ten or 15 biopsies must be made and out of these one, two, and sometimes

three are carcinomas Schiller feels satisfied if in 100 cases he finds one carcinoma

The iodine test is neither painful nor difficult nor expensive. If it could be carried out systematically on all women Schiller claims we could extend the probability of a 96 per cent healing to all carcinomas of the cervix

Treatment - The treatment of carcinoma of the cervix at the Memorial Hospital, New York, is discussed by W P Healy and E L Frazell 32 Carcinoma of the cervix comprised 2494 per cent of all cancers in females admitted to the Memorial Hospital This was 1116 per cent of all cancer admissions This report shows but slight increase in the percentage of early cases The routine use of the Schiller test and the colposcope may bring some improvement, but those who have used these tests are not uniform in their commendations At the Memorial Hospital, however, they rarely see cases which require these refinements of diagnosis as the diagnosis is usually obvious when the patient is referred

Radiation has been the method of choice in all cases of cancer of the cervix for the past 20 years

During the last two decades, many changes have been made in radiation methods for the treatment of cervix cancer First, radium alone was used, in in the form of the element and placed against the lesion or into the cervical canal Later it also was applied externally about the pelvis in the form of radium packs Credit is due the late Dr Harold Bailey for established methods of cross-firing the diseased area by radia-Still later, bare glass tubes containing the radium emanation were implanted in the periphery of the cervix in order to give a more uniform dose This method was discarded when we learned how to make the gold filtered radon seeds in use today. In 1922, external radiation in the form of low-voltage roentgen therapy in combination with the direct application of radium, was introduced as a routine procedure in our clinic In 1926. high voltage roentgen therapy represented by the 200 k v. machine was instituted. This voltage has continued to be our standard to the present For a short period of time in 1931, and 1932 a few patients were treated by roentgen rays generated at 700 kv peak The number. however, was too small to be of statistical value, even though the encouraging results obtained would suggest that supervoltage machines may have distinct value in selected cases These forms of external radiation are used in an effort to increase the amount of effective radiation delivered to outlying parts of the pelvis not affected by radium applied to the cervix

During the years under consideration in this report, 1 e, 1928 to 1931 inclusive, the usual procedure consisted of a preliminary cycle of roentgen therapy delivered through four pelvic portals measuring 15 by 10 cm. One portal was treated daily with a dose of 750 r The physical factors were 200 ky (peak), 4 or 30 ma, 50 cm TSD and ½ mm cu filtration The beam was directed toward the parametrium so that this region was cross-fired without crossfiring the bladder and rectum author considers this method of crossfiring of the parametrium to be of extreme importance. Within a week or ten days a radium treatment of 1500 mc hr was given directly against the cervix by means of a vaginal applicator called the "bomb" This applicator could also be directed in such a way as to irradiate either or both fornices in a similar The following day an intramanner cervical and intrauterine application of 3000 mc hr was given This form of applicator consisted of two radium capsules of unequal strength arranged in tandem within a rubber tube which was inserted into the cervical and uterine canal The lower capsule was twice the strength of the upper one In cases having bulky papillary and pedunculated lesions, the snare cautery was used to remove excess disease before the radium application Antiseptic douches administered daily greatly aid in clearing up the infection and reducing the foul vaginal discharge These douches also aid in preparing the site of disease for the application of the radium

Since 1933, the authors have used the divided dose method of roentgen therapy while the radium applications have remained the same By this method we have increased the dose to the parametria from 1 to 25 erythemas. This has been made possible by the addition of the two lateral pelvic fields and an increase of the total dose. The filter has remained the same but the target skin distance has been increased to 70 cm. Instead of the 750 r dose per portal which they formerly gave at one treatment, they now treat two opposite portals daily with doses of 200 to 250 r. A total of 1500 r. per portal can be tolerated without permanent skin damage if given over a period of 21 days

In classifying the cases as to clinical stage of disease the authors prefer the League of Nations system. They vary from it only in that they use the descriptive terms, early, borderline, advanced, and palliative instead of Groups 1, 2, 3, and 4. The criteria are essentially the same.

League of Nations Classification

Definition of Stages-

Group 1—The growth is strictly limited to the cervix uteri. Uterus mobile

Group 2—Lesion spreading into one or more fornices with or without infiltration of the parametrium adjacent to the uterus, the uterus retaining some degree of mobility.

Group 3—(a) Nodular infiltration of the parametria, on one or both sides extending to the wall of the pelvis, with limited mobility of the uterus or massive infiltration of one parametrium with fixation of the uterus.

- (b) More or less superficial infiltration of a large part of the vagina, with a mobile uterus
- (c) Isolated metastases in the pelvic glands, with a relatively small primary growth
- (d) Isolated metastases in the lower part of the vagina

Generally speaking, all cases not falling into Groups 2 or 4 will be placed under Group 3

Group 4-(a) Cases with massive infiltration of both parametria extending to the walls of the pelvis.

- (b) Carcinoma involving the bladder or rectum
- (c) The whole vagina infiltrated (rigid vaginal passage) or one vaginal wall infiltrated along its whole length with fixation of the primary growth
 - (d) Remote metastases

Complications—These may be early or late

Late radiation changes in the bladder have received considerable attention. They vary from congestion to actual ulceration of the bladder mucosa. The resulting cystitis is frequently severe and may last a long time. It is often complicated by calcific deposits.

Radiation proctitis is similar to the changes noted in the bladder. It manifests itself by bloody mucus, diarrhea, and severe rectal pain

Pyometra of greater or lesser degree is fairly common. It occurs in retro-

verted uten where drainage is poor and in those in which the cervical canal becomes obstructed by tumor or radiation changes. Dilatation of the cervical canal and irrigations of the uterine cavity may clear up the condition but often hysterectomy is required

A few patients develop pelvic peritonitis following radiation treatment. This is usually due to a reactivation of an old pelvic inflammatory condition.

Fistulas developing as a complication are serious, they may be vesicovaginal, rectovaginal, or a combination of the two varieties, and are usually a manifestation of advanced disease rather than excessive radiation

Fundal Carcinoma

Treatment—Observation of the treatment of the fundus of the uterus is discussed by L. C. Scheffey and W. J. Thudium ¹³. The authors summarize their studies as follows.

- 1 Four out of five women with carcinoma of the fundus developed it after the age of 50, in three out of four it was postmenopausal in onset
- 2 Irregular uterine bleeding was the predominant symptom. Discharge and pain were of minor diagnostic significance.
- 3 The advantage of diagnostic curettage outweighs its potentiality for harm. This is especially true of those patients who may develop carcinoma prior to the menopause when more obvious pathology notably fibromyoma uteri, may appear to be the predominant lesion.
- 4 Carcinoma of the fundus should be graded as to its degree of malignancy, but as simply as possible. While the folly of attempting to base a prognosis entirely on the gradation of the cell type of the growth is obvious, it is plausible to believe that careful consideration of the stage of differentiation of the tumor cells,

together with the clinical features of the case, is of distinct value in planning treatment and evaluating survival chances.

- 5. The best results, regardless of the type of treatment, were obtained in the low grade malignancy group *Radiation* alone gave the best end-results when all groups were considered, and was particularly efficacious in the intermediate and high grade groups. When *surgery* was employed the results were better when it was combined with radiation
- 6 The ultimate prognosis depends upon factors other than the grade of malignancy Primarily they are clinical and relate to the age and physical condition of the patient, the duration of symptoms, the promptitude of diagnosis, and the extent of the disease Secondarily, they relate to treatment Surgery alone has definite limitations, it should prove more efficacious when combined with radiation

While radium therapy in carcinoma of the fundus, either alone or in combination with x-ray, offers much and has proved its worth, the carefully considered objections that have been voiced by Sampson are based on rational grounds. These objections may possibly be overcome, in part at least, by more effective intrauterine radiation.

Chorionepithelioma

B Zondek³⁴ discusses the diagnosis of chorionepithelioma by the gonadotropic hormone test of the urine. That the demonstration of an increased excretion of gonadotropic substance in the urine is important for early diagnosis of chorionepithelioma is now acknowledged unanmously. While the increased excretion of gonadotropic principle usually ceases about one week after delivery of a normal placenta, it may continue for from 4 to 12 weeks following discharge of a hydatidiform mole.

The author recommends the following procedure In case the pregnancy test is still positive six weeks after the discharge of a hydatidiform mole and the content of gonadotropic factor in the urine increases progressively during this time, it is probable that a chorionepithelioma is present. Quantitative assay for gonadotropic substance is especially important in such cases If a positive pregnancy test can be obtained at the same time with spinal fluid (undiluted or diluted), this is further confirmation of the diagnosis As a further diagnostic safeguard. a carefully performed exploratory curettage is necessary In case histologic examination of the curettage material is doubtful, which may sometimes be the case, assay of the urine for gonadotropic factor is of greater significance in the diagnosis than the histologic examination

In case the pregnancy test has become negative following discharge of the hydatidiform mole, the patient's urine should be assayed at monthly intervals. If the negative reaction becomes positive again, the following possibilities must be considered. Either there is a new pregnancy on the patient has a chorionepithelioma

In early pregnancy the content of gonadotropic substance amounts to an average of 10,000 mouse units per liter of blood and from 5000 to 30,000 mouse units per liter of morning urine duction of gonadotropic principle may also be increased in gestation toxicosis in such a fashion that amounts near those obtaining in hydatidiform mole may be discharged in the urine The increased excretion therefore indicates the presence of a hydatidiform mole only if toxemia of pregnancy can be excluded symptoms of toxicosis are clinically so clear that an error should not arise from this source Chorionepithelioma does not occur until weeks or months have passed after discharge of the placenta or a hydatidiform mole.

If there is no toxicosis and if the content of luteinizing factor amounts to more than 200,000 mouse units per liter of morning urine, it is likely that a hydatidiform mole is present. One assay is insufficient, however. The more the content of gonadotropic substance increases in the course of observation the more certain will diagnosis become. The spinal fluid should also be examined. If the pregnancy test (reaction II or III) can be obtained with undiluted or diluted spinal fluid, this may be important support for the diagnosis According to the author's35 present experience a diagnosis of hydatidiform mole is made if at least 200,000 mouse units of luteinizing factor is present in a liter of urine on repeated assays, and if in addition at least 416 mouse units per liter is present in the spinal fluid

If a patient has discharged a hydatidiform mole and thereafter the pregnancy test has become negative, to become positive again in the course of several weeks, the presence of at least 416 mouse units of luteinizing factor per liter of urine, in case a new pregnancy can be excluded, will in itself indicate a diagnosis of chorionepithelioma A similar amount in spinal fluid confirms the diagnosis. The hormonic diagnosis of chorionepithelioma is not difficult, for the reason that the content of luternizing substance in the urine is usually far more than 416 mouse units per liter (up to 1,000,000 mouse units per liter)

Irradiation Therapy

An excellent treatise on irradiation for malignant disease of the genitals is presented by A. N. Arneson ³⁶. Its chief uses are

1 Carcinoma of the Cervix—Carcinoma of the cervix is a disease that

may be considered as moderately radio-In most clinics surgery has sensitive been abandoned for patients with that disease and treatment is given by radiation alone No single method is suitable for the treatment of all patients, and in some instances it may be impossible to make a satisfactory application of radium. The most suitable distribution of radiation will be obtained from an intrauterine tandem combined, whenever possible, with some method for delivering radiation into the vaginal fornices lateral to the cervix The so-called colpostat is used most frequently for that purpose

Some means other than radium applied to the cervix must be employed in the attempt to treat adequately the outlying tumor-bearing regions, such as external irradiation by roentgen rays. Taussig performs lymphadenectomy after irradiation, or at the time radium is used. The radium treatment consists of a cervical application or the insertion of gold seeds into the regions occupied by the various lymph glands. In some instances both methods may be employed.

The amount of external irradiation that must be delivered in the attempt to treat adequately the disease in the outlying tumor-bearing regions will produce an crythema of a rather marked degree in the irradiated skin fields, and some constitutional reaction in the patients receiving the dose. Due to the fact that the parametrial regions the adjacent lymph glands are involved in most instances, the administration of roentgen rays is just as essential as the application of radium to the cervix.

There are certain advantages to be gained if the treatment of a cervix case is begun with x-rays. By this means any existing infection will be diminished, which in turn will reduce the degree of reaction and the incidence of complications from the radium may be facilitated

by regression of the size of the primary lesion.

Roentgen treatment can be administered in single exposures to each pelvic field, or a divided dose technic may be used

It is essential that patients be observed at frequent intervals during a course of divided dose treatment. The regression of the primary lesion should be observed carefully. In some instances, due to the marked shrinking and stenosis of the cervical canal, it may be necessary to interrupt the external irradiation and apply radium. The reappearance of actively growing tumor noted in serial biopsies taken within the first two weeks following roentgen treatment indicates that, whenever possible, radium should be applied within that period

The average intrauterine tandem used in the treatment of cervix cancer consists The strength of the of two capsules lower capsule (cervical portion) is usually about twice that of the upper one. The tandem should be applied so that it is surrounded completely by the cervix with the lower end about level with the external os, or the most dependent portion of the primary lesion Various intravaginal applicators can be used also, depending upon the gross character of the lesion in question. After the application the vagina is distended with gauze packing to increase the distance of the bladder and rectum from the radium in order to protect those structures from excessive An indwelling catheter can be used to keep the bladder collapsed so that it will receive a minimum of exposure

The full amount of the radium treatment may be administered by means of a single application, or, as was noted for x-rays, the total dose may be divided into several treatments given a few days apart. For a number of years Healy has delivered the full amount of radium radi-

ation within 36 to 48 hours Due to excessive reactions he has, during the past few years, employed the intravaginal applicator in one position only, which is usually against the cervix. On the following day a tandem is inserted into the uterus for a dose of 3000 mg hr. The tandem is of sufficient strength to deliver that amount of radiation within about 24 hours Six weeks after the radium treatment, the cycle of x-rays is repeated, unless a divided dose technic had been employed for delivering a large amount of roentgen radiation before the application of radium

At the Radiumhemmet (Stockholm), the radium treatment is divided usually into three applications. The first two are separated by an interval of one week, and the last is given three weeks later. Complete treatment, therefore, requires about four weeks.

It is interesting to note that the various technics employed for applying radium to the cervix at the Memorial Hospital (Healy), the Radiumhemmet (Heyman), and at other institutions, have produced about equal clinical results. The absolute five-year cure rates have ranged from 20 to 22 per cent.

2 Carcinoma of the Corpus—Surgery has proved to be an efficient method of treatment for early cases of corpus cancer. However, all patients with operable lesions cannot be treated by hysterectomy, because the disease tends to occur in elderly women. Some authors advocate radium and x-rays for all cases of this disease.

For all cases treated by irradiation, including both operable and inoperable lesions, cure rates of from 32 to 36 per cent have been shown. Among patients with operable lesions, from 47 to 54 per cent have survived the five-year period. In every large series the cures from hysterectomy have been from 56 to 59

per cent. It is interesting to note that among patients who might be considered suitable for surgical treatment, Heyman has reported a relative cure rate of 64.3 per cent for irradition alone.

In many clinics both radiation and surgery are combined in some instances. Postoperative irradiation has been used extensively. Preoperative treatment has been employed less frequently, and it is feared by many that the use of x-rays or radium would increase the technical difficulties of an operation performed at a later date

In the radium treatment of corpus lesions it is difficult to determine the size and location of the tumor. The disease may form a bulky mass that will distort the cavity so greatly that radium cannot be applied in a manner that will deliver a suitable distribution of radiation. Approximately 20 per cent of the cases are complicated with myomas that may also distort the cavity The danger of the radium capsule acting as a piston to force blood containing tumor cells through the lumina of the tubes into the peritoneal cavity is emphasized by Simpson There is also the danger of perforating the uterine wall if pressure is made during the insertion of radium against a portion of the myometrium that is infiltrated by the disease

The average dose of radium employed in the treatment of corpus cancer ranges from 3500 to 4500 mg hr. The application may be made during the first two weeks following external irradiation. For a number of years, Healy has employed both radium and x-rays in many patients before the uterus was removed six to eight weeks later. In more than 50 per cent of the removed uters, there was no evidence of viable cancer.

3 Carcinoma of the External Genitalia—The malignant lesions of the external genitalia are chiefly epidermoid

carcinomas of an adult type that are relatively radioresistant. The disease tends to occur in elderly women among whom the tissues about the vulva are easily damaged, and usually show abnormal changes that are already present. Those regions will not tolerate the amounts of radiation required in most instances. As a result, the use of radiation has usually been limited to patients who were inoperable due either to the extent of the disease or some associated constitutional condition.

For the double-sided Basset operation, Taussig reports an operability of 75 per cent, and a primary mortality of only 46 per cent. In a series of 23 patients treated by that method he obtained a five-year cure rate of 65 per cent, and among 12 patients 55 per cent survived ten years. Those statistics are probably among the best that have been given for vulval cancer.

4 Carcinoma of the Vagina—Carcinoma of the vagina has been cured rarely by surgery alone. For radiation, Healy reports a five-year cure rate of 12 per cent. In 129 irradiated cases he cited from the literature, 12.4 per cent survived that period. The soft, friable, vascular lesions of the cauliflower variety usually show the greatest response to radiation. Only palliative results can be obtained in the large annular lesions filling the vagina. Fistulas into the bladder or rectum are fairly common sequelae, if the primary lesion is located in the vesicovaginal or rectovaginal septum.

Treatment should be given with both x-rays and radium. A protracted roent-gen treatment with multiple exposure totaling 1500 to 2000 roentgens to each area will usually produce considerable regression in the size of the lesion. Following this procedure various plaques, or other intravaginal applicators containing radium, can be used at distances of

about 10 cm for doses ranging from 1000 to 2000 mg. hr.

5 Ovarian Tumors — Whenever practical the patients are usually treated surgically. Tumors that prove to be malignant are given postoperative irradiation

For irradiating ovarian tumors the entire abdomen should be included. It is usually necessary to employ upper and lower abdominal areas on both the anterior and posterior surfaces. The operative scar should be included in the direct beam, due to the frequency of recurrences in that region from implantation metastases. Complete treatment will usually require from two to three weeks. During that time from 1000 to 1500 roentgens can be delivered to each area.

OVARY

Simple Cysts of the Ovary

Diagnosis—E V Stabler37 selected 93 patients for his discussion because their symptoms seemed to relate directly to the ovary, both preoperatively and postoperatively Follicular, luteum and retention cysts were generally the rule All the patients had cystic ovaries that were diagnosed at the time of operation Two symptoms were common to all cases a boring type of pain in one or both sides, and an increase of pain at menstruation, of a bearing down type Fifty-five patients had pain in the back, 53 had pain down the leg, 58 had regular menstruation, 23 had irregular menstruation and 37 had to go to bed because of pain at the menstrual period

Treatment—His treatment was the resection of the ovary, removing all cystic tissue, removal of the entire ovary if the whole ovary was cystic, both ovaries if both ovaries were cystic Postoperatively results, which range from six years

to four months, show freedom from pain in 47 cases, pain after operation that corresponded to the resected ovary in 32 cases, pain after operation that corresponded to the removed ovary in 15 cases, and pain after operation believed to be due directly to the remaining ovarian tissue in 23 cases. The regularity of menstruation improved in 33 cases, menstruation was unimproved in 17 cases, the menstrual cycle was shorter and the flow more moderate in 60 cases. 41 patients were apparently improved and five were apparently unimproved Recognition of, or the failure to recognize, the clinical importance of multiple follicular, luteum or retention cysts of the ovary may result in the success or failure of a major surgical procedure as far as the clinical results to the patient were concerned

Rupture of the Ovary

Diagnosis—More than 300 cases of ovarian rupture of the corpus luteum causing intraperitoneal hemorrhage have been reported to date. The clinical and pathologic features of this condition are described by S. Leon Israel³⁸ who reports ten additional cases.

Sudden trauma may be responsible Corpus luteum perforation has occurred following an abdominal blow, during quiet sleep, during coitus, and during the performance of ordinary activities, such as walking, dancing, and washing clothes

The amount of free blood found in the peritoneal cavity after ovarian rupture may vary from one-half ounce to several liters. If the origin of the hemorrhage is a perforated graafian follicle only serosanguinous fiuid may be present, but frank bleeding usually occurs when a richly vascularized corpus luteum ruptures A characteristic relationship exists between the time of ovarian rupture and the menstrual cycle. Follicular rupture occurs at approximately mid-interval and corpus luteum rupture during the last half of the cycle. All ten of the corpus luteum perforations presented occurred during the premenstruum.

The clinical manifestations of ovarian perforation may be either sthenic or asthenic, varying with the size of the perforation and the degree of hemorrhage. The patient with asthenic symptoms may appear quite comfortable, despite the considerable amount of free blood within the peritoneal cavity. The sthenic type, on the other hand, may be introduced by violent pain of shock. Between both extremities, all gradations of the acute abdomen may be present.

The erroneous diagnosis of acute appendicitis is frequently proposed, more especially in follicular rupture. The sudden onset of abdominal pain, nausea, vomiting, fever, leukocytosis, and tenderness in the right iliac fossa characterizes both conditions. The erythrocyte sedimentation rate may be a diagnostic aid, inasmuch as it is usually normal in appendicitis, and increased by intraperitoneal hemorrhage. The presence of a palpable adnexal tumor favors the diagnosis of ovarian rupture.

The sthenic variety of ovarian rupture is usually diagnosed as ruptured ectopic (tubal) pregnancy

Treatment—The advisability of operation depends upon the individual case If appendicitis or ectopic pregnancy can be definitely excluded from the diagnosis, nonoperative treatment may be applicable in many instances of ovarian hemorrhage

The patients exhibiting signs of marked hemorrhage require immediate operation. If shock is present, supportive measures (including blood trans-

fusion, intravenous infusion of glucose solution, and external heat) are necessary adjuvants. The incision should be lower midline or paramedian. Whenever possible, the bleeding ovary should be conserved. The simplest procedure is to strip the hematoma cavity of its lining and approximate its walls with a fine catgut suture. Wedge shaped resection of the ovary or oophorectomy may be required, if the bleeding is uncontrollable with sutures.

PSYCHOTHERAPY IN GYNE-COLOGICAL DISORDERS

The intimate relationship of psychotherapy to gynecological practice is discussed by M. D. Mayer 39

Some examples of leading symptoms which may be more or less influenced by psychic processes are

- 1 Amenorrhea This may be a symptom of a variety of mental conditions ranging from an acute and temporary fear through various degrees of hysteria to the severest psychosis
- 2 Menometrorrhagia There is ample evidence that irregularity in the amount and time of the bleeding may result from mental causes

The onset of menstruation as well as its cessation is often associated with psychic disturbances.

Some of the facts found in disturbances at the menopause are the fear of growing old and dving, which is mobilized by the cessation of bleeding, the fear of losing attractiveness, losing the partner, disturbing his potency, and loss of libido, the realization of the impossibility of further childbearing, and the unrealistic, unconscious wish to have more children, converted into hysterical symptoms, often involving the gastro-intestinal tract

- 3. Pelvic Pain—Among the clinical pictures frequently met with in the group under discussion are included dysmenor-rhea, dyspareunia, ovarian neuralgia, some cases of mittelschmerz, and certain paresthesias, of which the most trouble-some one is pruritus vulvae. One may also include the right-sided pain often found in young single adolescents, so often associated with a masturbation conflict and so often operated upon for chronic appendicitis.
- (a) Dysmenorrhea continues to be a baffling symptom, even when we exclude the women with pelvic tumors, displacements, endometriosis and detectable hormonal disturbances, a great number of sufferers are left. In some of these psychogenic factors are contributory of determining
- (b) The majority of cases of dyspareuma coming to the gynecologist are primarily psychogenic, although all cases have some psychologic factors

For practical purposes the treatment of psychogenic dyspareuma may be divided into

- .1 Initial Dyspareunia of which there are the mild, the severe, and the extremely severe forms
- In the mild type, there is a somewhat excessive reaction to an unfavorable situation as, for instance, an inept, inexperienced husband, an unusually thick hymen a timid individual, the patient is co-operative and has insight In these cases the treatment can be rapid and one can very well combine local treatment with psychotherapy method embodies the dynamics of the psychotherapeutic cure without any attempt to give the patient conscious insight In this respect it is similar to many forms commonly used in medical treatment but differs in that the physician is more aware of the mechanism

At the first visit the patient is interviewed (mostly listened to) and preferably not examined When an examination is eventually made, it is but an inspection. There should be no pain. The doctor gets the woman's confidence

An endoscope is inserted through which a wick of medicated gauze is passed and left in At subsequent visits very gradual mechanical dilatation combined with the local application finally permits the easy introduction of the smallest vaginal speculum This is replaced by a series of graduated test tubes up to 11/4 inches (3 17 cm) in diameter Then the patient is shown how to introduce this test tube herself, which she does with ease. Then she is given the test tube and instructed to introduce it herself at home for several days husband is interviewed and instructed. and all treatment tentatively discontinued before the couple make any attempt at coitus

- B Acquired Dyspareunia In the group resulting from fear of pregnancy one may combine a brief psychotherapy with adequate contraceptive advice. In the group in which the dyspareunia is a result of a negative reaction against the husband local treatment is of no avail. Brice psychotherapy of the suggestive type is almost always doomed to failure
- C Pruritus Vulvae—Some cases of pruritus vulvae which defv all other means of treatment respond to intense psychotherapy. Unconscious masturbation in a sexually frustrated individual is, of course, the most common mechanism, yet saying so, bluntly, is of no use and often has unfortunate results
- 4 In the field of contraception psychotherapy is of obvious importance. The widespread practice of coitus interruptus is no doubt compatible with mental and physical health in many men

and their mates, somewhat dependent upon the degree of control in the case of the man, and the rapidity of orgasm in the woman On the other hand, it is often associated with disturbances in the form of neurasthenia or psychoneurosis When long-continued, especially when associated with premature ejaculation, the chronic pelvic turgescence in the woman without deturgescence may result in subjective fullness, pain, dragging sensations, paresthesias, and may actually lead to the objective signs of thickening, shortening, and tenderness of the uterine ligaments Many of these women can be considerably helped by a change in their contraceptive technic combined with instruction, encouragement and psychotherapy of their partners Proper contraception is an important factor in many cases coming to the psychotherapist

Failure to cure sterility, or, in lieu thereof, to adjust by means of adoption or substitutive gratifications, may result in tragic consequences

- 5 Frigidity, from the gynecologic standpoint, can be divided into the primary and the acquired types. The prognosis is far better in the latter group.
- 6 Certain examples from the field of obstetrica require mentioning. In the vomiting of pregnancy we have an example of an intricate interlacing of conscious and unconscious mental factors with nervous, hormonal, and chemical ones.

The gynecologist, then, should know psychotherapy for the following reasons

- 1 To be able to elicit a psychanamnesis
- 2 To avoid certain difficulties in the case management of sick women
- 3 To know when to supplement his gynecologic therapy with psychotherapy

- 4 To use the latter prophylactically, as in premarital instruction
- 5. To understand the dynamics of many of his medical and surgical cures
- 6 To know when and when not to recommend formal psychotherapy such as analysis

VAGINA

Vaginal Plastic Operations (Local Anesthesia)

Treatment-It has been the custom of R I. Furber and A R H Duggan⁴⁰ for 18 years to inject into the superficial tissues a 1 350,000 solution of epinephrine hydrochloride in physiologic solution of sodium chloride when doing vaginal plastic operations The procedure climinates the continuous drip method, maintains a clear field (which favors greater accuracy of dissection and suturing) and diminishes loss of blood The original method of the continuous drip allowed a large volume of saline solution to flow over the operative field, carrying away an unknown and often large quantity of blood from the dissected tissues. The solution spreads in a natural plane of cleavage, and dissection is greatly facilitated. For a cystocele of average size about 10 cc of solution is required, and a similar amount for an average cervical repair. It has been suggested that reactionary hemorrhage and delayed union or malumion of the tissues might follow the use of such Furber and Duggan have a method watched carefully and have never experienced the former, and they have been unable to observe any change in the uniting powers of the tissues in several Their share of secondhundred cases ary hemorrhages has been no more than that experienced by most gynecologic surgeons

BLADDER

Urinary Antisepsis

Henry W E. Walther⁴¹ presents an evaluation of the drugs employed in urinary antisepsis. No single drug for all types of infections in the urinary tract is satisfactory. The author discusses the various agents employed.

1 Oil of Santal—Historically this drug has been held in high regard from remote times as a specific for gonorrheal urethritis. Oil of santal is excreted in the urine partly unchanged and partly as a compound of glycuronic acid. It is thought to have a specific action on the staphylococcus, which may apply to cocci in general

The Council on Pharmacy and Chemistry of the American Medical Association in its 1936 edition of Useful Drugs recognizes oil of santal but recommends the restriction of its use in gonorrhea to the subacute and chronic stages, in which its irritant action may stimulate healing Although less popular than formerly, oil of santal and the other related volatile oils still have a place in urinary antisepsis

2 Methenamine - Treatment with methenamine without constant control of the hydrogen ion concentration is likely to be unsuccessful At pH of g, urine with a 05 per cent concentration of methenamine rarely sterilizes itself at the end of 24 hours At a pH of five urme can be sterile after four hours at 986° F $(37^{\circ}$ C) This agrees with the author's observations that the pH should be below 5 6 if a sufficient amount of formaldehyde is to be generated in the urine The old idea that methenamine and an acidifier should be given separately has proved fallacious, the custom of giving them together is now universal, without the gastric irritation that was supposed to result

- 3 Methylene Blue Methylene blue is undoubtedly the best known of the group of the diphenylamine dyes, in which are found methylene blue. gentian violet, acriflavine and mercuro-Methylene blue became very popular during the last decade of the nineteenth century, being turned to good account in gonococcic infection. It also found a peculiar application in tuberculous conditions of the urinary tract Methylene blue is not so inert as many hold it to be It is bactericidal even in comparatively high dilution. Its irritating effect on both the digestive and the urinary systems must be borne in mind
- 4. Acriflavine-Its antiseptic action begins within two hours after oral administration and lasts for at least eight hours Unlike most of the other urinary antiseptics, its action is more pronounced when the urine is alkaline Hence to promote efficiency sodium bicarbonate is generally given at the same time the author's clinic it has helped to clear up the urine in cases of renal and vesical infections in about 50 per cent of the cases In nearly all our cases there were disagreeable gastrointestinal disturbances if treatment was kept up for any length of time, and this was equally true when sodium bicarbonate was administered with it
- Therapy—On the whole these dyes have been found a most valuable adjunct in the majority of the cases in which die were used, but sometimes they failed utterly, thus proving the truth that there is no single bactericide that will destroy all bacteria in the urinary tract. Their sphere of usefulness is a wide one, owing to the fact that they work equally well in an acid and an alkaline medium. They require no special dietary regimen. They have a soothing effect on the inflamed mucous

- membrane A large part of their usefulness lies in their capacity to penetrate the tissues and to attack the bacteria The author has in their own habitat found the results better in renal and prostatic infections than in cystitis and urethritis. He advocates doses of 0.2 gm three times a day, to be continued for a longer period according to the chronicity of the infection as well as the tolerance of the individual patient Dye therapy should not be prolonged indefinitely in many of these cases, as the majority of patients past the age of 50 with urinary infections have more or less impairment of the digestive and hepatic tracts It is well to alternate periods of medication with rest periods During the latter, he forces the fluid intake. If there is no improvement in seven days the treatment will not prove useful
- 6 Hexylresorcinol—It is chemically stable, nontoxic in therapeutic doses, nonirritating to the urinary tract, bactericidal in high dilution in urine of any reaction and is excreted by the kidnevs unchanged in sufficient percentage to impart active bactericidal properties to the urine In addition, it is susceptible of being administered by mouth, secreted in the urine at a rate which admits of continuous local action in the urinary tract, and finally the urine secreted possesses a bactericidal action against organisms exposed to it, and not a mere growth-inhibiting property chronic infections of the urinary tract in adults, due to staphylococcus albus and aureus and in some strains of bacillus pyocyaneus, oral administration of hexylresorcinol, without any other treatment, has resulted in prompt and complete disinfection of the urinary tract, accompanied by clearing up of the urine and disappearance of symptoms colon bacillus infections more persistent

a rule, local treatment will be found necessary, as well as intensive courses of the drug. The authors made it a rule in all cases to discontinue any form of treatment that gave no evidence within seven days of producing useful results.

7 The Ketogenic Diet—In 1932 Clark, and also Helmholz working independently, tried for the first time the effect of acidification of the urine by feeding a special type of high fat, low carbohydrate diet designed to produce a state of ketosis. A low calory or starvation diet would serve equally well to produce ketosis, by forcing patients to consume their own endogenous fat. It is well known that the body will call on this supply whenever energy of diet falls below the expenditure of energy. Production of ketosis then depends on madequacy of available dextrose.

On account of the marked gastrointestinal disturbances caused by the ketogenic dict, it became increasingly difficult to persuade patients to take it. In view of the larger percentage of elderly patients with urosepsis, and with established gastrointestinal disorders, the problem was far from being solved by the ketogenic dict, which seemed at best a clumsy roundabout way of producing a high degree of acidity that might be achieved in some other way.

8 Mandelic Acid- In 1935 Rosenheim announced his discovery that mandelic acid would do in a direct way what had been done in an indirect and complicated way with beta-hydroxy butyric acid and the ketogenic diet. After trying and rejecting several other similar agents, he chose mandelic acid because it is a hydroxy acid, it is nontoxic, and it is excreted unchanged in the urinary tract, which it renders bacteriostatic. He recommends that it be given in the form

of a salt such as sodium or ammonium mandelate

This treatment has a tremendous advantage over the ketogenic diet in that the patient may eat whatever he likes This new product is unpleasant to the taste and often causes the gastrointestinal upsets so common to many of the urinary antiseptics now in use. Rosenheim showed that, given orally, mandelic acid escapes metabolism or conjugation in the animal organism and is excreted by the kidneys in the urine in a concentration sufficient for bactericidal action, provided the hydrogen ion concentration is lowered at the same time

9 Sulfanilamide—H F Helmholz⁴² recently made observations with sulfanilamide which demonstrate that urine of patients taking the drug develops definite bactericidal power for such organisms as are commonly found in infections of the urinary tract Those urines containing escherichia coli and aerobacter aerogenes vielded the most striking results, however, with streptococcus aureus and streptococcus faecalis, five strains of organisms out of 11 were killed in from 24 to 72 hours after incubation Proteus vulgaris and pseudomonas aeruginosa, in eight strains studied, give positive cultures, demonstrating that the action of sulfamilamide was less effective here

J E Dees and J A C Colston⁴³ are the first to record their experiences with sulfamilamide in the treatment of gonococcic infections. In 19 cases observed the smears and urines became negative for gonococci in two days in five cases, in three days in five cases, in five days in two cases, and in four, six and 23 days respectively in single cases. In one case, smears became negative on the ninth day, positive on the fourteenth day and again negative on the seventeenth day. In three cases gonococci were still present after 11

days All patients received, in four divided doses a day, 48 gm of sulfanilamide daily for two days, 36 gm daily for three days, and then 24 gm daily for from four to eight days. They warn against a continuance of the drug immediately on complaint by the patient of headache, fever, lassitude, cyanosis, general malaise or extreme weakness.

ENDOMETRIOSIS OF COLON AND RECTUM

Treatment—Among 104 patients with endometriosis who have been treated at the Lahey Clinic, 17 have had involvement of the sigmoid, colon or rectum (163 per cent) R B Cattell⁴⁴ divides these cases of endometriosis into three groups, which are based on the extent of the involvement of the intestine and the indications for treatment (1) Endometriosis of the rectovaginal septum, (2) endometriosis involving the serosal and muscular coat of the intestine owing to its juxtaposition to a generalized endometriosis in the ovaries, tubes or uterus, and (3) endometriosis involving the entire intestinal wall All three groups may show obstructive symptoms. although in the third the obstruction is more marked and is more readily confused with carcinoma. In patients with rectovaginal involvement a biopsy to establish the diagnosis should precede the abdominal operation. If the rectovaginal involvement is extensive and is producing a severe obstruction, a bilateral oophorectomy is indicated, with or without colostomy Colostomy, if done, is temporary and can be closed after a few months

The treatment of the cases with involvement of the rectosigmoid and rectum due to extensive endometriosis in the pelvis is radical so far as the uterus, tubes and ovaries are concerned. The

author has felt it advisable to remove the endometrial cysts encroaching on the lumen of the intestine, as well as the ovaries, although the dissection of the cyst on the intestine is likely to be tedious and time consuming if one is to avoid injury to the intestine. No resection of the intestine was performed nor was a colostomy necessary in this group of eight patients. The treatment of discrete implants involving all layers of the sigmoid is a more difficult problem, owing to their infrequent occurrence and their similarity to carcinoma

All four patients in this group (3) were operated on because of intestinal obstruction One patient was submitted to an abdominoperineal resection because of a diagnosis of carcinoma (the ovaries were not removed), two had a modified Mikulicz type of local resection since their condition was suspected of being endometriosis at the time of operation (the ovaries were removed in one) and the fourth patient had a bilateral oophorectomy without resection of the intestine In a more recent case in which a solid tumor of the cecum was found. a frozen section diagnosis of endometriosis was of value. In this patient there was no obstruction, so bilateral oophorectomy was done and the cecal tumor was left in situ. In the presence of an intestinal obstruction that is not severe, it seems safe to remove the ovaries without resecting the intestine if the diagnosis of endometriosis is confirmed by frozen section Resection should be carried out in patients in whom caremoma cannot be excluded. If the diagnosis is not certain and resection is performed, and if examination of the resected specimen shows that the lesion is an endometrial implant, the ovaries should be removed

The results of the surgical treatment of endometriosis are and should be satis-

factory. There has been no operative or subsequent mortality in the 17 cases in which intestinal involvement was present Of the five patients in the first group three have no remaining tumor, one has no symptoms although a small mass remains and the fifth patient was treated after biopsy by x-ray therapy and is unimproved. In group two, five patients are free of symptoms, but, in spite of removal of both ovaries, barium sulfate enemas show narrowing and spasm of the intestine

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OBSTETRICS

By P Brooke Bland, MD, and Arthur First, MD

TOXEMIAS OF PREGNANCY

Predisposing Factors—J P Peters¹ reports 351 patients with late toxemias of pregnancy and discusses the predis-

posing factors One hundred and fifty patients had satisfactory records, of these only 15 had no relevant disturbances preceding their first toxemias It

is safe to assume that at least some of the patients who had inadequate histories had suffered some disease which helped prepare the ground for the toxemia. Forty-two patients with pyelitis or pyelonephrosis were found Thirty-six other patients, while suffering from pyelitis during pregnancy, developed hypertension or edema, 22 showed evidence of renal or vascular disease varying from albuminuria or nephritis to renal calculi, two had pre-existing arterial disease manifested in one by hypertension and in the other by chorioretinitis From the histories alone, from 45 to 47 patients out of 150 had definite renal or vascular disease before the pregnancies in which toxemia first occurred Approximately ten per cent of the patients had a history of rheumatic fever or chorea, most of them showing signs of heart disease Acute respiratory infections preceded the toxemia in 16 instances In view of the infectious origin of nephritis and of pyelitis, the possibility that infection plays a significant part in the toxemias of pregnancy should be more thoroughly investigated, although the infectious theory has been discounted during the past few years. In general, the predisposing factors appeared to be renal and vascular disorders and the diseases that cause such disorders

As to recurrences, at least 40 per cent of the patients developed toxemia in subsequent pregnancies Eclampsia, as well as the other forms of toxemia, whichever way they may be classified, far from conferring immunity, tend often to recur Of the total 351 patients, 148 were not traced One hundred and twenty, or 34 per cent, are either dead or victims of chronic disease, and 69, or 20 per cent, have had further toxemias At best, but 46 per cent survive in good health and only 15, or seven

per cent, of those traced are free from disease.

As far as the saving of life is concerned, the present methods of treatment are adequate when properly applied, but the injury to the renal and vascular systems is nearly always made manifest in subsequent pregnancies, which cause further permanent damage. Therefore Peters concludes that pregnancy should be prevented in women with such pre-existing disease or in those who have had previous toxemias, and terminated on the appearance of symptoms if pregnancy occurs

Pernicious Vomiting

Treatment - Suprarenal cortex therapy in the vomiting of pregnancy is advocated by W. Freeman, J. M. Melick and D K McClusky² who report 78 cases treated The hormone was dispensed in tablets and ampules, equivalent apiece to 3 grains ($0.2\,\mathrm{Gm}$) of dried adrenal cortex. The tablets were taken orally, while the ampules, containing 1 cc of solution, were administered either intramuscularly or intravenously Hormone therapy was resorted to only after the ordinarily accepted remedies, such as alkalies, fruit juices, hypodermoclyses, and the like, failed to give relief It must be emphasized that only the Armour product was used

The tablets were given to 31 patients who were merely nauseated or who vonited but rarely or at regular intervals. All members of this group were ambulatory and were self-administrators of the drug. They were told to take one tablet three times daily, about one-half hour before their regular meal. If at the end of a week their symptoms had not completely ceased, the dose was increased up to six tablets a day. The use of the tablets was continued until the entire contents of a bottle of 100 were

taken In only one instance was it found necessary to prescribe more than one bottle for any patient

The hypodermic route was prescribed for 47 patients who vomited at irregular intervals or who vomited everything taken by mouth The contents of one ampule (1 cc) were injected three times a day, about one-half hour before the regular mealtime. The injections were continued thus for three days after the disappearance of all signs of vomiting, then one ampule was replaced by one tablet on each successive day, so that by the end of the sixth day after cessation of vomiting, the patient was receiving three tablets a day and no ampules The use of the tablets was then continued until 100 had been taken Ambulatory patients were given the injections by the district nurse, relatives, or friends, or even took them themselves

Of the 47 treated patients with less severe nausea and vomiting, only two, or 43 per cent, failed to receive any benefit from the hormone. There were 15 patients who had severe nausea and vomiting and 16 patients who were classed as having pernicious vomiting. A cure was effected in every instance within from three to five days with the parenteral treatment. It is important to note that in no instance did the condition of nausea and vomiting become more severe, necessitating the interruption of pregnancy.

In the more severe cases of nausea and vomiting, the body fluids and vitamins were replaced as rapidly as possible in those patients in whom the ketosis did not clear as rapidly as their chinical symptoms, insulin was added to their intravenous medication

The authors conclude that suprarenal cortex is an efficacious and important therapeutic weapon in combating the types of vomiting due to pregnancy

Vomiting of Pregnancy

W. Sussman³ advocates the use of parathyroid extract for early nausea and vomiting of pregnancy His patients were divided into two groups. All patients in both groups were on a diet high in carbohydrates, low in fat, and with restricted condiments. The patients in Group 1 were given orally about 40 grains (259 Gm) of calcium daily, usually in the form of phosphate, and 10 cc of a ten per cent solution of calcium gluconate intravenously at varying intervals The patients in Group 2 were given the calcium orally and 100 units of parathyroid extract in some cases intramuscularly and in others intravenously every two or three days A few of the patients in the second group were also given calcium gluconate parenterally

The author believes there is a definite superiority of parthyroid extract plus calcium over calcium alone and over the usual accepted therapy, as there is a shortening of the duration of the early vomiting of pregnancy by this treatment

Eclampsia

Treatment-1' Rucker4 discusses the treatment of eclampsia His method consists of four principles, namely (1) stopping the convulsions, (2) good nursing care with emphasis on rest, (3) promoting kidney activity, and (4) digitalis Magnesium sulfate, intravenously has been remarkably efficient in stopping convulsions His initial dose is 20 cc of a ten per cent solution Frequently he gives a second dose of 15 cc and occasionally a third dose of 15 cc. In a few cases he uses $7\frac{1}{2}$ grains (0.5 Gm) of sodium amytal intravenously. He prefers the magnesium sulfate to the sodium amytal, because the former wakes the patient up when it stops the convulsion and the latter puts her to sleep. In such an event it is hard then to know whether

the patient is comatose or simply drugged. Nevertheless, sodium amytal is a drug to have around, because occasionally one drug will control the convulsions when the other will not

Under the head of good nursing care comes the avoidance of external stimuli, such as bright light, noises and jarring the bed The patient should be kept on her side to lessen the chance of aspirating vomitus and other fluids in the mouth The tongue should be protected during the clonic stage of a convulsion, and the nurse should be prepared to give artificial respiration if it should be necessary. Too much emphasis cannot be placed on rest For this reason he is opposed to colonic irrigations, gastric lavage and purgatives These patients are desperately ill and need all the rest they can get

The prognosis is better if the patient is putting out a good quantity of urine Usually he gives water or cream of tartar lemonade to promote kidney activity. The best way to give fluids to an eclamptic patient is by the stomach. If the patient is not awake enough to drink, one can slip a nasal tube into the stomach and pour in a pint of fluid every eight hours. When there is anuria or marked oliginal dextrose intravenously is given varying the strength according to whether there is much or little edema present.

Digitalis has a definite place in the treatment of eclampsia. Half a cat unit dose is given as soon as possible after the magnesium sulfate or sodium amytal. He has never seen edema of the lungs when digitalis has been given

Concerning delivery or terminating pregnancy this has no place in the treatment of eclampsia. The patients who go into labor should be treated as conservatively as possible, which means in most cases episiotomy and low forceps

under local anesthesia. When ante partum eclampsia is relieved and the patient is putting out a good quantity of urine, then comes up the question of terminating pregnancy. Unless one has exceptionally good control of the patient, it is unwise to let the patient leave the hospital undelivered. No eclamptic or recent eclamptic patient should have a general anesthetic

A series of 129 consecutive cases of eclampsia have been treated with an uncorrected maternal mortality of 4 65 per cent

An excellent outline of the various methods of treatment of eclampsia is given by W J Dieckmann.⁵ The treatment of eclampsia, in general, has been divided into surgical and medical

Surgical Treatment-The surgical treatment consists of the immediate termination of the pregnancy by cesarean section, vaginal hysterotomy, or by manual or instrumental dilatation (accouchement force) of the cervix, followed by version and extraction only large clinic in which eclampsia is still treated by immediate delivery is the Berlin Frauenklinik, supervised by No recent figures for their maternal mortality are available, but others who practice immediately delivery have reported a mortality rate as high as 23 per cent, and less experienced physicians may have a mortality rate of 48 per cent as reported in one city

Medical Treatment — The medical treatment may be divided into two large groups, as follows

Stroganoff or Sedation Method Large amounts of morphine and chloral hydrate are administered. Any necessary manipulations are performed under chloroform anesthesia. Venesection and early, but not forcible, delivery through the natural passage are advised.

Rotunda Hospital or Elimination Method: Colonic irrigation, purgation, starvation, and the parenteral injection of one per cent sodium bicarbonate solution are the essentials of the original treatment. The use of morphine and venesection has been added. Labor may be induced only after three days' treatment.

The treatment which is used at the Chicago Lying-In Hospital and which, with perhaps minor changes, is used in many other clinics, may be termed the "combined method" because the essential parts of the various methods have been systematized for certain definite purposes

General Treatment-The patient is placed in a quiet, cool, darkened room Constant observation is necessary to prevent injury to the tongue, falling out of bed and aspiration of vomitus or drowning from the occasional excessive pulmonary secretions. A mouth gag (clothes pin, tooth brush) and tracheal catheter should be at hand. A catheter should be kept in the bladder until the patient is definitely improving. The temperature, pulse and respiratory rate, urine volume, and blood pressure should be determined every two hours until the patient is conscious and improving. The period is then lengthened to four hours and later the intervals are increased still further. The patient's condition as to the number of convulsions, the degree of coma, the quality of the pulse, difficulty in breathing, evanosis, etc., should be noted

Convulsions—Since all drugs are toxic in the doses necessary to control the convulsions, we prefer to use several simultaneously. Smaller amounts are, therefore, required and the undesirable effects of each are minimized. A number of hypnotic drugs are mentioned because all are not always available. We prefer

magnesium sulfate and luminal sodium. If the case is protracted, chloral hydrate is used

Morphine — One-fourth grain (16 mg) is given on admission and repeated at hourly intervals until the convulsions are controlled or the respirations to ten per minute

Magnesium Sulfate—Ten cc of a 25 per cent or equivalent amounts of a 50 per cent solution are injected and 5 cc of the former solution are given after each convulsion or until a total of 30 cc has been given

Luminal Sodium — Five grains (032 Gm) are injected subcutaneously and, if necessary, repeated in 12 to 24 hours

Chloral Hydrate — Thirty grains (2 Gm) are given in 100 cc of starch water (one tablespoonful of starch to 100 cc) by rectum and repeated as necessary

Elimination—A soapsuds enema is used and should be repeated until a satisfactory bowel movement has been obtained. If the patient is vomiting the stomach is emptied with a nasal tube but no cathartic is injected. Sodium sulfate (Glauber's salt), 1 to 1½ oz (30 to 45 Gm) is a safer purgative than magnesium sulfate.

Hypertension—The blood pressure, at least in part, is compensatory. All sedative drugs lower it, but the barbiturates and chloral hydrate are the most efficacious in reducing it or in preventing further increases.

Renal and Cerebral Symptoms— The oliguria or anuria, coma, fever, tachycardia and cerebral edema are treated with injections of hypertonic glucose solution. Five hundred to 1000 cc of a 20 per cent solution are given intravenously over a period of 30 to 50 minutes and this amount is repeated every six to eight hours, if necessary. The temperature of the solution at the needle point must be 100° F (37.7° C) This can be achieved by immersing at least three feet of the rubber tubing in water at a temperature of 104 to 106° F. (40 to 41.1° C). Within four hours after the injection the urine volume should equal at least 60 per cent of the volume injected. Sufficient glucose solution is given to insure a urinary output of at lease 30 cc per hour and should be continued during the postpartum period until the normal diuresis begins If the 20 per cent concentration does not produce a diuresis, 500 to 800 cc of a 30 per cent solution are used. If there is an anasarca or if there are symptoms of cardiac failure, 300 to 500 cc of a 30 per cent, or 100 to 300 cc of a 50 per cent solution are given. We have never seen any injurious effects if the glucose solution is properly prepared and administered.

Pregnancy—While the various procedures outlined above are being carried out, the period of gestation, size of fetus, and irritability of the uterus are determined. No attempt to start labor or terminate the pregnancy should be instituted until the eclampsia is under control, which usually requires six to ten hours.

Antepartum and Intrapartum Eclampsia—It there is cephalopelvic disproportion, a cesarean section should be performed when the eclampsia is under control. This presupposes that the case is not actually or potentially infected.

Severe Eclampsia—Over 35 Weeks' Gestation If there is no disproportion and if the cervix is effaced and soft, labor should be induced by rupturing the membranes, care being taken to drain off as much of the ammotic fluid as possible, and, if necessary, inserting a bag Pituitrin in doses of one or two minims or preferably pitocin may be given subcutaneously every 30 minutes until the interval between contractions is two or three minutes and the duration of each

is 40 to 50 seconds But if the cervix is long, firm and closed, a cesarean section should be performed if the environment is suitable.

Severe Eclampsia—Under 35 weeks' gestation The cervix will, as a rule, be uneffaced, firm and closed In general, labor should be induced as described in the preceding paragraph.

Mild Case — Any period of pregnancy: No operative procedure should be carried out Labor should be induced only if the cervix is soft and partly dilated. If the patient is not delivered, she must be kept under close observation until the pregnancy is terminated, because if the eclampsia recurs it is usually of the severe type and is quite often fatal.

Postpartum Eclampsia—The treatment is entirely medical

Diet—If the patient is conscious or as soon as the stomach is emptying itself, as indicated by a failure to aspirate water which has been previously injected, a ten per cent solution of **Karo syrup** is injected through the nasal tube at hourly intervals. The initial amount is 50 cc and is increased by 50 cc amounts up to the patient's tolerance (usually 200 to 300 cc.) These feedings are continued until the patient is able to take the eclamptic diet which consists of water, fruit juices and fruit. The fluid balance must be watched carefully and kept negative

Miscellaneous Procedures — The withdrawal of 500 to 1000 cc of blood may be necessary if acute cardiac failure and pulmonary edema develop Spinol puncture is rarely if ever indicated and then only if there are signs of a markedly increased intracranial pressure. The blood pressure should be watched carefully. Occasionally, it drops before delivery and many require treatment. After delivery a 10 to 15 pound weight (sand

bag) should be placed on the abdomen and a tight binder applied for 8 to 12 hours to prevent vasomotor collapse. If the latter occurs, *ephedrine*, ¾ grain (48 mg) every two to four hours, hypertonic *glucose solution* and occasionally *blood transfusions* are necessary *Atropine* in doses of ½100 grain (06 mg) should be given if there are many râles. Up to ½30 grain (2 mg) may be given within one hour if pulmonary edema occurs *Oxygen* should be administered by nasal catheter if the patient is cyanotic

Anesthesia — Operative procedures can be performed quite often without any additional anesthesia because of the large amounts of narcotics already given. If additional anesthesia is necessary, local infiltration with novocaine solution is preferable.

Sequelae—A study is presented by H M Teel and D E Reid⁶ of 173 patients with eclampsia who were treated at the Boston Lying In Hospital during the 20-year period from 1915 through 1934. The uncorrected mortality was 26.6 per cent. The mortality for patients who had attended the clinic prior to the development of eclampsia was less than for those admitted as emergencies. The mortality was higher in multiparas than in primiparas and was also higher in patients over 30 years of age.

Of the 127 survivors of eclampsia eight have subsequently died, three of recurrent pregnancy toxemias, two of severe hypertension with cerebral lesions, one of cardiac decompensation, probably of vascular origin, one of lobar pneumonia complicated by hypertension and possibly chronic nephritis, and one of cancer of the cervix Eighty of the patients who survived the eclampsia have been followed from more than one to 21 years. The average follow-up interval is 7.6 years. The incidence of hyperten-

sion among these patients was 27 5 per cent, and the incidence of albuminuria 875 per cent Evidence of significantly impaired renal function was found in only one case.

The patients were studied in groups with reference to their past histories as these concerned hypertensive disease and nephritis prior to the eclampsia A significant number of them had hypertensive disease or nephritis prior to the eclampsia, and both the immediate and remote outlook for these patients was considerably poorer than for those known to have been normal before the eclampsia Of the 29 patients followed who were known to have been healthy prior to the eclampsia the incidence of subsequent hypertension was 103 per cent and that of albuminuria was nil Such symptoms as were encountered at follow-up exam mation was largely explicable on the basis of hypertensive disease

The authors found that eclampsia is frequently complicated by pre-existing hypertensive disease and less commonly by chronic nephritis

The immediate mortality of uncomplicated eclampsia they noted is much lower than when it is superimposed upon pre-existing hypertensive disease of nephritis

The most common abnormal finding at follow-up study in patients who have had eclampsia is hypertension. In this series of cases its incidence was 27.5 per cent. The incidence of albuminum at follow-up study was 8.75 per cent. These figures do not represent the true incidence of these two findings as sequels to eclampsia, for hypertensive disease and, less commonly, nephritis were sometimes present before the eclamptic pregnancy. Of 29 posteclamptics followed who were known to have been healthy prior to the eclampsia, none had albuminum or evidence of impaired renal function,

and only three (103 per cent) showed hypertension

Such damage as occurs as a result of eclampsia would appear to be primarily vascular in character Chronic parenchymatous nephritis, and significantly impaired renal function was uncommon sequelae

COMPLICATIONS OF PREGNANCY

Heart Action

H. J Stander and K Kuder⁷ discuss the treatment of heart disease complicating pregnancy. It is most essential according to these investigators that in every maternity hospital all pregnant patients with heart disease be studied in a special cardiac clinic throughout their antepartum period Every pregnant woman who comes to register at a hosortal, clinic or physician's office should have a careful and complete examination, in which particular attention is paid to the heart. Too often is this neglected, and the patient proceeds to term with an unrecognized but easily demonstrable licart disease. The possibility of a cardiac lesion is one of the many reasons, and an important one, that all pregnant women must see a physician as early in pregnancy as possible. It is the author's practice that when heart disease is suspected or diagnosed the patient is immediately referred to the special cardiac clinic, where a thorough re-examination is performed. Should the condition warrant it, the patient is admitted to the hospital for a complete study of her cardiac condition, otherwise she is followed at frequent intervals in the cardiac clinic

In general, patients with class 1 or class 2a heart disease can be safely cared for in the office or antepartum cardiac clinic until about two weeks

before term, at which time they should be hospitalized. This statement, however, should not be taken too literally, as each patient must be treated individually, as symptoms or signs may develop that make it imperative to admit to the hospital a class 2a and sometimes even a class 1 cardiac patient, a month or more before the expected date of delivery The pulse and respiration rates are among the best indications as to the behavior of the heart Undue fatigue, palpitation, dyspnea and chest pains are further signs of which a careful note and record must be made An untoward development in any one of these is sufficient cause to hospitalize and provide forced rest in bed-the best treatment for most of these cases. The patients in class 1. and many of those in class 2a, will deliver spontaneously after two weeks' rest in the hospital, without undue rise of the pulse and respiration rates during labor However, it is well to use forceps on full dilatation of the cervix in a certain number, the maternal pulse and respiration rates being used as the main index for such intervention. A pulse rate of over 110 and respiration rates of 28 or over are sufficient reasons to save the patient the further strain on the heart incidental to the voluntary muscular work of the second stage of labor. It must be emphasized that any anesthesia producing partial asphyxia, such as nitrous oxide, is contraindicated in the delivery of cardiac patients. The authors prefer ether anesthesia administered by the open drop method, for all cardiac patients

In patients belonging definitely in class 2b and class 3, much earlier and longer hospitalization is essential. It is often necessary to readmit the patient to the hospital two or more times during the pregnancy. An analysis of the hospital admissions of 418 cardiac patients.

reveals the fact that of this number, 22 women had 136 hospital admissions before delivery, an incidence of approximately six admissions per patient Forceps delivery, to obviate the second stage of labor, is performed far more frequently in these patients. The use of digitalis compounds is of great help, in their experience, in preparing these patients for the ordeal of labor This may also be said for those patients in whom they perform cesarean section because of the heart condition. When the patient is definitely in class 3, the treatment is more radical than in the class 2b patient When there has been a definite break in compensation either prior to or during the pregnancy, they generally advise cesarean section with sterilization Such patients are admitted to the hospital early in pregnancy, adequate rest and digitalis therapy is provided and the section is performed when the patient has attained her optimum condition and no further improvement appears possible The operation is performed under open drop other anesthesia and in the presence of a competent internist. During the past four and one-third years they have performed such cesarean sections on patients definitely in class 3 and have lost only one mother Of course it is not advisable to allow some of these class 3 cardiae patients to proceed to viability and therapeutic abortion or miniature cesarean section becomes the treatment of choice. In 418 cardiac cases, therapeutic aboution for the heart condition was performed in 12

An analysis of the past history as well as careful questioning of their 418 cardiac patients revealed the astounding fact that 189, or 498 per cent, of them were wholly unaware that they had cardiac disease. This finding further impresses us with the absolute necessity of a careful heart examination on every

pregnant woman at her first visit to her physician.

The important factors in the handling and treatment of cardiac disease in pregnancy are:

- (a) All pregnant patients must consult their physician early in pregnancy
- (b) A thorough examination, including the heart, must be made at the time of the first visit
- (c) If the past history, symptoms, signs or examination reveal heart disease, however mild, the patient should be followed in a special cardiac clinic or by her physician in consultation with a competent internist
- (d) All pregnant patients with cardiac disease must be in a hospital during the last two weeks of gestation and must be delivered in the hospital
- (e) Patients with class 1 and 2a heart disease may be delivered spontaneously, provided the pulse and respiration rates are not markedly augmented or no untoward symptom or sign such as dyspnea or cyanosis develops, in which event it is advisable to obviate the second stage of labor by the application of forceps on full dilatation of the cervix
- (f) Patients in class 2b and class 3 should be hospitalized early in pregnancy in order that as accurate an evaluation of the cardiac reserve as possible may be made in order to decide whether or not the pregnancy should be allowed to proceed
- (g) Should it be deemed advisable to interrupt the pregnancy, it becomes the obstetrician's further responsibility to decide whether a therapeutic abortion followed by birth control, a therapeutic abortion followed by tubal sterilization or a miniature section with sterilization is the proper treatment. This decision will depend on a number of factors, such as the age and parity of the patient, the duration of the pregnancy, the number

of living children, the desires of the patient and her husband and, lastly but most important, the severity of the cardiac involvement

- (h) On the other hand, should it be deemed advisable to let the pregnancy proceed to viability or full term, the patient may have to remain in the hospital for months or be readmitted several times during the pregnancy in order to maintain a careful and vigilant watch over the cardiac condition. It may be necessary to digitalize the heart and to continue digitalis therapy
- (1) The treatment, when viability or term is reached, in this relatively small but important group of patients will depend on the cardiac condition in each individual. When there has been a history of definite cardiac failure and the heart is now compensated, it is their practice to perform a cesarean section with tubal resection. In the other patients in this group it is usually advisable to deliver by forceps.
- (1) No anesthesia producing varying degrees of asphyxia should be used in cardiac patients, at the time either of delivery or of operation. Open drop other anesthesia has given the best results
- (k) Cardiac patients who are first seen or admitted to the hospital in labor with acute heart failure must be placed in an oxygen tent and delivery effected as soon as possible, but consistent with sound obstetric principles. So far they have delivered none of this group of patients by cesarean section. Cardiac stimulants such as ouzbain, are, of course, of the utmost assistance in these patients.

K Harris⁸ has observed 100 pregnant women suffering from valvular disease of the heart with normal rhythm during pregnancy. No patient died during the course of pregnancy or labor. In the management of such a case a careful

investigation of the history of the patient's exercise tolerance before and during the early months of pregnancy is of great importance. Early breakdown of exercise tolerance in a primipara is a grave sign, since death may occur soon after labor or congestive heart failure is likely to supervene with its attendant grave risks. In multiparous women the experience derived from the previous pregnancies is of great value, since the breakdown of exercise tolerance earlier and earlier in each successive pregnancy is a serious feature for the same reason.

The subsequent mortality was greater in those patients in whom congestive heart failure occurred than in those in whom it did not, and particularly in the primiparas. When congestive failure developed early in the pregnancy the patients did well, possibly as a result of obstetric treatment, those in whom the failure developed late did badly, particularly if the failure had not cleared up at the time of delivery. A short interval between pregnancies increased the risk of congestive failure in a cardiac case.

The incidence of premature delivery was increased in cases in which congestive failure developed during pregnancy, whereas it was not increased in the other cardiac cases. Patients with slight or no enlargement of the heart did better than those with moderate or considerable enlargement. There appeared to be no difference in the prognosis between cases of mitral stenosis, those of aortic regurgitation and those in which both these lesions were present.

Pregnancy is contraindicated in those patients with heart disease with normal rhythm, who have ever had congestive failure, in whom the exercise tolerance broke down early in a previous pregnancy or in whom the heart is considerably enlarged. Termination by empty-

ing the uterus should be undertaken as soon as the failure has been relieved by rest and other medical measures. During the pregnancy careful supervision and increased rest with admission to the hospital for at least two weeks before the onset of labor is advisable

Weight Changes

M D A Evans⁹ maintains that there is very little variation in weight during the first trimester, some patients losing a little and others gaining, depending probably on the ease with which the body adjusts itself to the presence of the ovum. The increase that occurs must therefore take place during the last six months.

The average monthly gain during the second and third trimesters should be between two and four pounds (09 to 18 Kg) and the total gain between 16 and 18 pounds (73 to 82 Kg) If the gain is greater, the patient should be questioned carefully and be examined in order to find, if possible, the cause of the discrepancy. In the 211 cases under consideration the average increase in weight of a potential toxemic patient was definitely more than that of a normal patient, but it was not sufficient to be of real clinical value, since the 4.3 pounds (2 Kg) that was found to be the average monthly gain of the toxemic patients was as a rule gained by the normal women during one of their later months It, however, the patient has a monthly gain of from four to five pounds (18 to 23 kg) in two or more consecutive months, it should be regarded as abnormal, dietetic errors, if present, should be rectified and a stricter supervision undertaken On the other hand, a sudden marked rise in weight during one month is of great help in foretelling a toxemia If the patient showed a monthly gain of eight pounds (36 Kg) or more, there was a 63 per cent chance of her developing a toxemia and, following a six to eight pound (27 to 36 Kg) gain, a 50 per cent chance

It would appear, therefore, that it is the sudden abnormal increase in weight rather than the gradual gain which is of importance in detecting an incipient toxemia This abnormal gain is as a rule an earlier sign than a raised blood pressure, but occasionally the latter is the first indication Therefore, ideal antepartum supervision should include the taking of the weight and blood pressure each month during the second trimester, permitting a diagnosis of toxemia of pregnancy before albuminuma appears Treatment could then be given and the percentage of the maternal mortality due to the toxemias of pregnancy should be materially reduced

X-ray in Primiparous Women

H Thoms¹⁰ emphasizes the advantages of applying the newer knowledge of pelvic variations to practical obstetrics and presents a survey of the results in 300 primiparous white women who have been delivered consecutively at full term in whom roentgenometry of the pelvis has formed a part of the antepartum examination. He has used roentgenometric methods almost as a routine for nearly four years, and he is convinced that their use has simplified many obstetric problems. For example, in none of the cases presented was "the test of labor" used and, from the fact that cesarean section was performed only six times in 300 consecutive primiparous women, it appears that radical measures were not substituted for the more conservative procedures

Exact dimensions of the pelvis as revealed by roentgenometry are not a substitute for careful obstetric judgment as developed by clinical experience. The

information thus obtained, like paint on an artist's easel, must be "mixed with brains". The employment of the contour of the superior strait as a basis for classification will allow all but the most abnormal pelves to be readily grouped. If other features of obstetric importance present themselves, such as the male type of sacrosciatic notch, narrow forepart, narrow subpubic angle, and forward displacement of the lower sacrum, these features may be noted. Every woman who is expecting her first baby deserves the advantages offered by roentgenometry of the pelvis.

Polyhydramnios

A Maver¹¹ directs attention to the fact that a severe hydrammon may cause considerable difficulties, such as severe dyspnea. If the signs of congestion become too severe, evacuation of the over large uterus by artificial termination of the pregnancy may become necessary. but the author suggests puncture of the hydrammon through the abdominal walls as another possibility. He thinks that the measure is indicated in serious signs of congestion with dyspnea. The technic is comparatively simple. The skin is disinfected and the puncture is made with a sterile trocar. The author usually makes the puncture about midway between the symphysis and the umbilious in the midline, because here are the fewest vessels and normally there are no intestinal loops in this region, so that the danger of damaging the intestine is excluded. In order to avoid injuries of the urmary bladder the puncture is preceded by catheterization Local anesthesia is used. The amount of amniotic fluid withdrawn varies between 850 and 3750 cc

The immediate result of the puncture was always good. The further course of the pregnancy varied. In order to avoid

labor pains, morphine or some other opium preparation was administered. Mild labor pain appeared in two cases but subsided again. In five cases delivery took place after one, three, six, eight and ten days, respectively, but in the other cases up to ten weeks elapsed before the termination of the pregnancy. The author never observed damage to the child.

Hemorrhage Complicating Early Pregnancy

I D Owen¹² states that gestation itself accounts for more than 90 per cent of vaginal bleeding in early pregnancy Spruck observed periodic vaginal bleeding (physiologic) with no demonstrable cause in 19 of 9000 pregnant women This bleeding approaching the normal menstrual flow. in both amount and duration, in only 05 per cent Pathologic bleeding not directly due to pregnancy may be caused by varicose veins, hemorrhage from a polyp, fibromyomas of the cervix, cervical erosion, carcinoma of the cervix, focal endometritis with ulceration, fibromyomas and pregnancy superposed on an adenocarcinoma of the uterus In pathologic bleeding directly due to pregnancy 50 cases of cervical pregnancy have been reported, the diagnostic triad of which consists of brisk vaginal bleeding, complete absence of uterine ciamps or pelvic pain and palpation of an enlarged pear-shaped cervix containing the embryo Evacuation with the finger should be attempted. If cervical dilatation cannot be accomplished easily or if the fetus is too large to remove through the partially dilated cervix, vaginal hysterotomy should be performed

Extrauterine pregnancy causes the death of 1000 women yearly in this country Tubal pregnancy occurs once in every 300 gestations. The history

of a skipped or delayed period, followed by vaginal spotting, suggests an ectopic gestation. Ectopic pregnancy occurs more often in multiparas and in women who have a scar in the iliac region. This fact suggests that these patients have had pelvic inflammatory disease or a corrective uterine operation which may be followed by prolapse, edema or kinking of the fallopian tubes. In hydatidiform mole, a lesion of the fetal portion of the gestational sac, vaginal bleeding is the commonest complaint.

Hydatidiform mole is a potentially malignant tumor. The immediate dangers are hemorrhage, perforation of the uterus and puerperal sepsis. The maternal mortality is ten per cent.

Chorionepithelioma develops in from five to ten per cent of patients who have had a hydatiditorin mole. About 45 per cent of chorionepitheliomas follow mole, 30 per cent follow abortion and the remainder follow ectopic gestation and labor at term

Placenta Previa

Diagnosis- | F McDowell¹³ presents nine cases of placenta previa in the last trimester of pregnancy in which the correct diagnos's was made in seven as a result of cystographic examination A cystogram was done on all patients who were admitted with a history of abnormal bleeding during the latter months of pregnancy or who came to the hospital not necessarily in labor but because of bleeding. The patient was first catheterized to empty the bladder completely They then used the technic as outlined by Ude and Urner with few minor variations From 30 to 40 cc of an opaque material, usually 12½ per cent sodium iodide, was then injected into the bladder and the catheter removed A flat plate of the lower abdomen with the patient in the supine position was then made. An

effort was made to prevent a tilting of either the table or the tube thus permitting the rays to pass straight downward. The first plate was then im mediately developed and read. If there was too much material in the bladder, as evidenced by an "overlapping" of the upper border, from 10 to 15 cc was removed and a second plate made. A large enough film was used to permit exposure of the entire pelvis and approximately half of the fetus

Criterion of Diagnosis-As noted by Ude and Urner there is normally a distance of about 1 cm between the fetal head and the upper margin of the This distance should be the same across the entire top of the bladder In the majority of the cases where a positive diagnosis of previa was made there was usually on one side the expected 1 cm (more or less) with a gradual or sudden widening out as the opposite side was approached, until a distance of sometimes 3 or 4 cm was obtained They considered this as suggestive of marginal placenta previa. A separation of from 2 to even 4 cm across the entire upper margin of the upper bladder and an associated suspicious history led them to consider the patient to have a complete or central placenta previa. It must be borne in mind that the presence of blood clots from a premature separation, which have settled into the lower uterine cavity, is capable of giving a similar picture, either of the marginal or central type. In either event the condition would in all probability be abnormal In all doubtful cases the plates were either repeated or the patient observed until she showed more definite signs of the condition

In their cases they observed that the cystograin was satisfactory only during the last trimester of the pregnancy, due to the fact that in earlier pregnancies

the head was still floating above the brim of the pelvis with the result that there was no pressure being made on the bladder It is better to have the patient in the early first stage of labor or at least have the head below the brim In the presence of prematurity the fetal head is not large enough to entirely fill the pelvis, with resulting unsatisfactory pictures The entire diagnosis depends upon the ability of the fetal head to exert pressure downward onto the bladder The amniotic fluid, acting as a transmitting agent, will then give the desired pressure on the urmary bladder, causing the even concavity of its upper border

Premature Separation

A plea for the conservative treatment of premature separation of the placenta is made by F. C. Irving 14. From Jan. 1, 1916 to April 1, 1937, 353 patients with premature separation were admitted to the Boston Laving-in Hospital, all beyond 28 weeks of pregnancy. These 353 cases are divided into two groups those with external hemorrhage and those with internal hemorrhage.

External Hemorrhage—There were 234 cases in this group. In the 170 patients delivered normally, by forceps or by the breech, in every instance only after full cervical dilatation, that there was no deaths. Labor was allowed to progress without interference If bleeding occurred before the onset of labor, contractions were induced in some instances by rupture of the membranes or by metreurysis. Of the total 204 cases delivered through the pelvis, five or 24 per cent received transfusions, as did an equal number, or 167 per cent of the 30 cesarean sections The increased frequency of transfusion among the cesarean sections indicates a greater blood loss than was the case with those women delivered through the pelvis

Of the 237 infants in this group, including three pairs of twins, 34 or 143 per cent were dead in utero when their mothers were admitted to the hospital Moreover, 40 others, or 168 per cent, although alive in utero, were under four pounds in weight when born. In almost one-third of the cases, therefore, salvage of the infants was either impossible or unlikely

Among the infants delivered through the pelvis the net fetal mortality was 7.5 per cent, while with cesarean section it was zero

Internal Hemorrhage — Bleeding which is entirely concealed is the exception, since in all but two of 119 cases of internal hemorrhage, there was some visible bleeding at some time Seventy. or 583 per cent, of 120 infants in this group were dead on admission and seven, or 58 per cent, were under four pounds In about two-thirds of the cases, therefore, there was little or no chance of saving the baby The net fetal mortality with pelvic operative delivery was 500 per cent, and the gross was 614 per cent. Under conservative treatment, the net mortality was 428 per cent and the gross was 88 1 per cent

For at least 20 years the method of controlling the hemorrhage approached by most American obstetricians has been by cesarean section. The results according to Irving have been far from good. An average mortality rate of 20.5 per cent is many times that of placenta previa, indeed there is no other fairly frequent complication of pregnancy, with the possible exception of eclampsia, that has been so often fatal. The woman with this form of internal hemorrhage is not only handicapped by acute blood loss, but she is also often the victim of shock caused by sudden distention of the uterus.

The patients are treated by rupture of the membranes, the insertion of a tight

cervical and vaginal pack and the application of a Spanish windlass abdominal binder, because Irving was discouraged by his results with cesarean section in these cases.

Among the 69 cases of internal hemorrhage subjected to cesarean section 19, or 27 5 per cent, required transfusion, as contrasted with four, or 11 7 per cent, of the 34 delivered by conservative measures

Since 1931 no patient with internal hemorrhage has been delivered by cesarean section unless the infant was living and viable and the mother in good condition. Twenty-six patients have been treated by the pack and Spanish windlass, with the one death, and eight others who entered in active labor have been left alone, with the exception of one case in which the membranes were ruptured artificially.

In the summary, therefore, it is noted that in 170 patients with external hemorphage delivered through the pelvis by simple means there were no deaths

In 30 cases of external hemorrhage treated by cesarean section, the death rate was 3.3 per cent

In 69 cases of internal hemorrhage delivered by cosarean section the death rate was 14.5 per cent

In 34 cases of internal hemorrhage treated by conservative measures the mortality was 2.9 per cent

Conservative measures, therefore, give a better prognosis for the mother in both types of premature separation of the placenta

In discussion of this subject, N W Vaux (*loc cit*) states that he divides premature separation into two groups

1 Those cases with mild frank bleeding, whose general condition and that of the infant *in utero* has not yet become affected by blood loss

2 Those cases which undoubtedly have concealed or frank hemorrhage sufficient to produce shock and collapse from blood loss. This is frequently seen in emergency cases, when the placenta has become completely detached and intrauterine fetal suffocation has occurred

The first group should be treated conservatively, for a time at least. In the second group the immediate treatment should be directed towards combating the shock and collapse, followed by prompt radical intervention.

In the last two years at the Philadelphia Lying-In Hospital he has felt that the proved cases of premature separation should be treated by immediate intervention by cesarean section, preferably under local anesthesia directly the opposite of the methods of conservatism advocated by Dr Irving It has been his custom, however, to use conservatism in the cases of mild or partial separation which evidence no results of excessive blood loss, but these individuals must be kept under constant observation, and the more radical methods employed if evidence of further separation presents itself

It is not appropriate to compare the conservative and radical policies on total groups of cases. The underlying etiologic factors, such as toxemia and associated conditions, must necessarily influence the method chosen and these affect the figures for certain methods of therapy.

Abruptio Placenta

This subject was presented by Couvelaire and by Weymeersch and Snoeck¹⁵ at the tenth gynecologic and obstetric Congress held in Paris. This discussion included not only retroplacental hematoma and resultant hemorrhage but also bleeding into the uterine wall, perhaps extending to all the internal genitalia and other viscera. The pathogenesis is not clear. It was thought to be related to nephritis and hypertension in multiparas beyond the age of 30, but it has been found that it is not dependent on vascular lesions or hypertension. The former play a part during pregnancy and then only the capillaries are involved Experimentally, these accidents appear to take place in women previously sensitized to various antigens, which makes them resemble the visceral infarcts by tolerance shock. The ovum does not take any part because the same phenomena can be produced in nonpregnant animals.

The incidence of uteroplacental apoplexy varies from 0.09 to 1.06 per cent according to various reports. The obstetric methods of treatment aim to empty the uterus as rapidly as possible. Surgical intervention includes conservative cesarean section (high or low) alone or followed by vaginal hysterectomy and abdominal hysterectomy. Obstetric treatment was employed in 853 of 1080 cases, with a maternal mortality of 6.58 per cent and a fetal mortality of 61.3 per cent. Surgical treatment in 227 cases entailed a maternal mortality of 21 per cent and a fetal mortality of 70.7 per cent.

The severity and extent of the hemorthages are not necessarily a criterion of the gravity of the case in deciding which of the three operative methods is to be selected. The time factor is the most im-If the uterus is emptied portant one during the first ten hours after appearance of the symptoms, the maternal mortality is 27 per cent. It rises to 40 per cent if the ten-hour period has been passed. Many obstetricians, in order to judge the functional value of the uterus, inject solution of posterior pituitary intravenously following cesarean section If the uterus contracts well, so that no late hemorrhage is to be feared, the organ is conserved. Clinically, the cases can be placed into two groups so far as treatment is concerned:

- 1. Hemorrhage preceded, accompanied or rapidly followed by the beginning of labor. In these, expectant treatment is the best. Morphine is given to relieve the pain, the bag of waters is ruptured, solution of posterior pituitary is given and eventually low forceps are used
- 2 Severe hemorrhage appearing before any signs of labor and the general condition indicating a probable uteroplacental apoplexy. Some recommended expectant treatment with artificial rupture of the bag of waters. Others, in severe cases, with marked shock and a toxic syndrome, feel that only operative intervention can be considered, preferably low cesarean section.

Complications Involving the Urinary Tract

Present-day maternity clinics turn out four types of infection cases for aftercare These are convalescing predelivery infections which have given no postpartum problems, second, infections involving the kidneys, which were not present during the pregnancy but took place during the puerperium, and third, cystitis cases without upper urmary tract involvement. These latter represent retentions and residuals following parturition where either intermittent catheterization or constant dramage has had to be employed and resulted in introduced infection. Fourth, pyelitis in pregnancy may also show pyelitis symptoms in the puerperium

At the Boston Lying-In Hospital all such cases are directed to the Out-Patient Department clinic where they are followed until recovery takes place, a subsequent pregnancy intervenes, as all too frequently happens, or the case is restudied because of failure of the infection to clear

The end results of urinary tract infections are reported by E G Crabtree in collaboration with C Prather and E L Prien ¹⁶

Postdelivery urinary cases are of four types Cystitis, pyelitis in pregnancy, pyelitis in the puerperium and those who have had pyelitis in pregnancy and also in the puerperium

The majority of cystitis cases recover in the first month after delivery. The majority of renal infections clear within four months after delivery

There is little difference in the rate of recovery among pyelitis in pregnancy, pyelitis in the puerperium and combined cases. They are best considered under the common heading "renal infection."

Renal infections which fail to clear within four months commonly do so because of four factors

- (a) Debility of the patient
- (b) Abnormal persistence of pregnancy renal changes
- (c) Abnormal persistence of pregnancy renal changes with anomalies or gross pathology
- (d) Bladder damage with residual urine

A previous history of cured urmary tract micetion without abnormalities of the urmary tract probably does not influence the incidence of pyelitis of pregnancy

Intections which are uncured at the begimming of the first pregnancy probably produce febrile pregnancies in most cases

Tolerance for infection either independent of pregnancy or associated with it seems to be acquired in many cases of long-standing infections. Such cases may be free from febrile symptoms during subsequent pregnancies or remain bacteriums.

If multiple infected pregnancies occur in a series of pregnancies they are apt to be in sequence. The majority of recurrent infections in pregnancies take place in uncured cases but there is a higher incidence than normal in these "cured" cases.

Any form of urinary tract infection, even cystitis, may give rise to febrile pyelitis in subsequent pregnancy

Infections which persist into the next pregnancy may remain symptomless bacteriurias, in spite of large renal and ureteral dilatations

Residual bladder urmes are not common in postdelivery cases even though the injury from which cystocele eventually develops must be present. Cystocele, therefore, probably develops slowly following birth injury.

Small bladder residuals, under one ounce, seem not to retard spontaneous recovery from infection. Residuals above two ounces probably are of significance

Children born of pyelitic mothers are not abnormal unless prematurity results from the severity of the infection

Maternal anemia due to urmary tract infection or other causes may harm the child during its first year, although it is usually born with a normal hemoglobin

Surgical Complications

The surgical complications of pregnancy are discussed by S. A. Cosgrove ¹⁷ These cases fall into three groups

- 1 Cases of appendicitis in the first seven months of gestation, in which all the mothers survived, as did all but three of the babies. All commentators agree that no disturbance of pregnancy is necessary thus early in pregnancy
- 2 Cases of acute appendicitis occurring in the eighth and ninth months of pregnancy or intrapartum
- 3 A small group of miscellaneous intra-abdominal surgical complications. The author's experience would not appear to lend much support to several of the factors of fear in relation to ap-

pendicitis in late pregnancy. Thus, in our several cases of ruptured appendix with peritonitis, drainage appeared to be just as effective and postoperative course just as smooth, as it could reasonably be expected to be in the nonpregnant.

The theoretic risk of infection of the undisturbed placental site is not, in his opinion, nearly so real as the actual risk of infecting the site should the uterus be opened transperitoneally, nor of infecting the broad lymphatic and cellular tissue areas exposed in extirpating the uterus

The fear of tearing the appendix or adhesions would appear to overlook the extreme mobility of all the abdominal viscera, and the possibility thereby of mutual accommodation to shifting relationship in spite of extensive inflammatory adhesions. This accommodation is so usual a part of the natural history of all intra-abdominal inflammatory states in relation to the natural functioning of all the viscera, that undue alarm concerning the equally natural functioning of the uterus is hardly warranted

So also the fear that "labor will follow operation within a few days with disastrous results" is not substantiated in his experience

The author concludes that acute appendicutes is a surgical condition invariably calling for prompt operative intervention

This indication is not modified but is even more promptly imperative when appendicitis complicates pregnancy, even at or near its termination

Its surgical treatment should not be combined with any manipulation to termmate pregnancy. This statement may be modified only by

(a) The legitimacy of simple procedure to expedite termination of the second stage of spontaneous labor.

(b) Recognition of the very rare possibility of concurrent serious factors of obstetric dystocia. When this occurs, recourse may be necessary to delivery by the abdominal route. But such interference should be reserved until after the onset of spontaneous labor, and an extraperitoneal approach selected.

Ectopic Gestation

Diagnosis — A. Mathieu¹⁸ stresses some of the diagnostic methods to determine the presence of a tubal pregnancy. Pain is an important symptom. There are eight types of pain connected with this condition, all explainable on a pathologic basis.

- 1 Acute lancinating pain coincident with rupture of the tube
- 2 Dull, constant pain associated with stretching and slow tearing of the tube before rupture
- 3 Crampy, almost constant pain caused by peristalsis of the tube and dilatation of the distal end of the tube during a tubal abortion
- 4 Soreness and tenderness of the entire abdomen caused by irritation of the peritoneum from the escaped blood
- 5 Phrenic or shoulder pain produced when the blood gets high in the abdominal cavity, under the diaphragm, and irritates the phrenic nerve endings (this pain is felt on either side or both sides of the neck)
- 6 Pain elicited by the deep muscle resistance that results when the palpating fingers sink deeply enough to cause pressure on the parietal peritoneum

When there is free blood in the abdominal cavity, palpation of the anterior abdominal wall is always pathognomonic. In such a patient the abdomen is usually not distended. There is generalized pain or soreness over the entire abdomen and with fairly light palpation the fingers will sink part way into the abdominal wall.

without resistance, only to be met by a rather doughy resistance as the fingers sink deeper. This tenderness is quite unlike that of the acute firm resistance and tenderness one finds in acute appendicitis with peritoneal involvement.

7 Pain produced by moving the cervix or the fundus

8 Generalized pelvic tenderness and produced by the palpating fingers

The character of the decidua is an important finding. It is a physiologic fact that wherever a pregnancy exists-be it in the uterus, the tube, the ovary or the abdomen-decidua is formed in the uterus, and when the fetus dies or when the pregnancy is disrupted the decidual lining of the uterine cavity is cast off and bleeding takes place This, in all but a few rare cases, is the cause Probably the of the uterine bleeding only time that blood regurgitates from the tube into the uterus is in the rare condition of interstitial pregnancy one patient, whose history and physical examination gave no suggestion of ectopic pregnancy a piece of tissue was seen emerging from the cervix which on examination proved to be pure decidua and contained no chorionic tissue. This finding induced the author to make a hysterosalpingogram, which showed a pregnancy aborting from the tube the contrary, the absence of decidual might mean nothing since the decidua may separate and pass out before the curettage takes place

The author also emphasizes the urobilinogen and icterus index tests as aids in the diagnosis of ruptured ectopic pregnancy. They are of distinct value in determining the presence of a hematoma or of blood in the process of absorption

Hysterosalpingography is stressed as a valuable aid in diagnosis. The author has used hysterosalpingography in several cases as an aid in diagnosis and has obtained practically 100 per cent correct diagnoses He has been able to visualize beautifully the abortion of the tubes (Figs 1, 2 and 3) and to establish what seems to be a pathognomonic x-ray sign (Figs 4 and 5) for a tubal pregnancy in the midportion of the tube. In cases of tubal pregnancy aborting from the distal end of the tube, the injected oil enters all the crevices between the aborting pregnancy and the wall of the distal ends of the tubes in such a way that it literally drapes itself about the mass and allows the oil-covered mass to be visualized by the x-rays

In his case of tubal pregnancy in the midportion of the tube the injected oil went down to the site of the pregnancy and, because this site was apparently well sealed off, ended abruptly and showed in a characteristic shadow. This also proved quite conclusively what has long been suspected by many—that the bleeding from the uterus in cases of tubal pregnancy is from the uterine wall and not from the site of the tubal rupture While he does not advise hysterosalpingography except when it appears necessary to establish the diagnosis, he does feel that the injection of iodized oil into the uterus and tubes in a case of tubal pregnancy is practically harmless case both tubes fill well and normally to their distal ends, one can surely rule out tubal pregnancy

Malignancy

In an effort to determine the effect of pregnancy on malignant tumors 54 patients with malignant tumors who were also pregnant were studied by F R Smith ¹⁹ The patients were grouped according to the location of the tumor, 1 e, genital, breast and nongenital

The rarity of the combination is best explained by the fact that the majority

of patients developing malignant tumors are beyond childbearing age, or in the last decade of childbearing

- A The author finds that pregnancy 15 detrimental to, and should be prevented in, patients having unarrested malignant tumors
- B Growing malignant tumors may be temporarily retarded by pregnancy but the growth is accelerated after the termination of the pregnancy
- C Pregnant patients with malignant tumors have a better prognosis
 - 1 If the pregnancy is not interrupted
- 2 If the pregnancy follows treatment of the tumor rather than occurring simultaneously with it. This is true whether the length of the life from the time of treatment of the tumor or the length of life from the beginning of pregnancy is taken for comparison. The latter gives a more accurate measure of the effect of the pregnancy upon the tumor.
- 3 If, in patients becoming pregnant after the tumor therapy, more rather than less than two years have elapsed since the tumor therapy
- 4 If in the breast and nongenital groups, the patient is not aborted regardless of the time relationship of the pregnancy to the occurrence of the tumor. This is possibly also true in the genital group but in the early months of pregnancy the patient is usually aborted by the tumor therapy anyhow. In this series no patient in the genital group became pregnant after the tumor therapy.
- 5 If the breast and genital tumors are treated before the end of the pregnancy. It is of distinct advantage to the patient to treat these tumors and ignore the pregnancy, but it is better for the patients with certain nongenital tumors not to be treated until the pregnancy is ended, especially with melanoma

D As to the stage of the pregnancy (using four months as an empirical borderline) when the patient was first seen. If the patient is aborted, there is some slight advantage in early over late abortion in the nongenital group, but a distinct disadvantage in the breast group and total. All groups fared better if not aborted, regardless of the stage of the pregnancy when first seen.

E As to Parity—Abortion was especially disastrous to primigravid women, whereas both primigravid and multigravid women did about equally well if not aborted

- 11 **Concerning the Fetus**—A Irradiation of breast and nongenital tumors in pregnant women has no tendency to produce malformed babies
- B In the genital group irradiation of the pelvic regions will usually produce abortion in the early months of pregnancy. This series sheds no light on the effect of the fetus of irradiation of the pelvis in the first half of pregnancy because no patient receiving such treatment went to viability.
- C In the latter months of pregnancy carcinoma of the cervix can be irradiated locally without affecting the baby or producing abortion
- D Of 41 known viable normal offspring at birth, only 25 could be traced. These show no evidence of any bad effects of tumor therapy at the present time (one to ten years of age)

Cervical Carcinoma—The frequency of carcinoma in pregnancy is estimated as 0 0321. The management of carcinoma of the cervix during pregnancy is discussed by W. C. Danforth. 20

Except in patients who are quite hopeless, treatment shall be immediately instituted without regard to the child unless the child has attained viability. The choice of treatment is important. If operative intervention is preferred the

type of operation must be chosen. If radiotherapy is elected a choice must be made between radium and x-ray, or perhaps a combination of these. A combination of surgery and radiotherapy may be wise. The fate of the fetus must be decided. And finally, intelligent management depends upon an appreciation, as definite as may be, of the extent of the growth

Operative removal is far more successful in early pregnancy. Vaginal hysterectomy will naturally find a restricted application because of the relatively small number of operators who can work with facility by this route.

In the first trimester, if operative management is chosen, radical hypsterectomy is at once to be carried out without previously evacuating the uterus. The disease and the pregnancy are then at once disposed of Previous evacuation increases somewhat the chance of diffusion of cancer cells. Operation should be followed by deep x-ray irradiation If radiotherapy is chosen (and, unless the cancer is an exceedingly early one), this seems the preferable course, irradiation should be done irrespective of the pregnancy. This should be followed by deep x-ray irradiation or by the radium pack it this is available. The fetus will be killed and will probably come away spontaneously. If it does not the uterus may be evacuated six to eight weeks later When x-ray is used, abortion is caused by alterations in the vessels of the placenta Abortion following radium and cord is usually due to the capsule in the cervix, which acts as a foreign body

In the second trimester, if the carcinoma is still operable, radical hysterectomy may be done if the surgical mode of attack is preferred. If irradiation is elected local irradiation by means of radium should be used followed by deep x-ray therapy. The fetus will be destroyed and may be expelled spontaneously later. If this does not occur the uterine body with its contents may be amputated, or if the extent of the lesion permits, complete hysterectomy may be done.

In the last trimester results of treatment are less satisfactory than in the earlier cases It is well to wait until the child has attained a development which renders extrauterine life fairly possible before beginning treatment, whether this is to be operative or radiotherapeutic This seems justified by the fact that at this stage of pregnancy the chance of permanently curing the mother by any means is not great. When this time has arrived, the uterus may be emptied and a subtotal hysterectomy done in short, a Poiro operation, with subsequent irradiation by radium and x-ray Baer's suggestion merits attention. Not over 3000 mg hours of local irradiation by means of radium may be given, which will check the growth of the cancer until the child is viable A Porro operation is then done, followed, after recovery, by complete radiotherapeutic treatment. This cannot be regarded as the best plan for the mother but will save an occasional infant. An alternative procedure is the radical Ries-Wertheim hysterectomy This is available only when the extent of the growth permits its use author's preference is for the Porio operation followed by irradiation

Treatment During Labor—(ases of cancer of the cervix in women in labor divide themselves into two groups, those in which the cancer is small and involves only a portion of the cervix, and those in which the cervix is extensively invaded. If a sufficient amount of normal cervix remains to allow enough dilatation to permit the passage of the infant without serious injury to the cervix, labor

may be allowed to complete itself spontaneously

Extensive carcinoma either obstructs delivery completely, or allows the passage of the infant only at the expense of tears of the carcinomatous cervix Serious hemorrhage, difficult or perhaps impossible to control, is the primary result with serious sepsis probable if the woman survives the labor If the cancer is sufficiently extensive to be in any sense a problem during labor, delivery should not be attempted from below. Incision or dilatation of the cervix is extremely hazardous and should not be attempted Two procedures are available A Porro cesarean section may be done, with complete radiotherapy later The operation will probably cause a wider diffusion of carcinoma, but it may be remembered that cure at this late stage of pregnancy is improbable in any event The removal of the uterine body lessens the danger of peritonitis, which is very likely to follow simple cesarean section Lochiometra is also prevented The safety of the infant is far greater than it delivery is done from below

Cesarcan section may be done, followed by a Wertheim radical hysterectomy. This can be considered only if the cancer is within operable limits. It is a tar more extensive procedure, and, in the greater number of cases, will not be possible. The Porro operation and subsequent irradiation are preterable. In patients operated upon too near the end of pregnancy the percentage of curability is so small that the assumption of a much greater primary operative risk does not seem wise.

PARTURITION

Artificial Induction

An analysis of 750 cases of induced labor from private practice is reported

by A Mathieu and A Holman ²¹ Their method of inducing labor is as follows:

At 7 A M an enema is given and at 730 pentobarbital is given, the dose depending on the patient's weight Patients weighing less than 130 pounds receive 75 gr (05 gm), those weighing from 130 to 150 pounds, receive 9 gr, and those weighing over 150 pounds, receive 12 gr The patient is asleep within 30 minutes. Then injections of three minims of pituitary extract are given and repeated every 30 minutes After the third or fourth injection, if labor has not started and if the membranes are still intact, thev are ruptured artificially unless there is some contraindications. The pentobarbital given before hypodermic injections are started saves the patient any discomfort or apprehension and keeps her tran quil In this series of 114 cases, in which pentobarbital was used preliminary to the induction, there were no failures and only five which required a second attempt There were no maternal deaths and the maternal morbidity was 53 per cent. The total fetal mortality was 35 per cent, and when two macerated fetuses were eliminated the corrected fetal mortality was 1.75 per cent

The authors believe that the maternal and fetal morbidity and mortality are not increased by induction

Induction of labor was successful in 98 per cent of the cases

Induction was apparently not responsible for the occurrence of any pathologic condition during labor, delivery, or the puerperium

In the last 550 inductions quinine was not used and the results were apparently not affected by its omission

In the last 351 cases, if labor did not start after three or four injections the membranes were artificially ruptured during induction if there were no con-

traindications and if they had not already ruptured The authors feel that this contributed markedly to the success of induction

In the last 114 cases castor oil was omitted and pentobarbital was given before the hypodermic injections were started. Omission of castor oil in no way affected the success of induction Pentobarbital has been advantageous in keeping the patient tranquil and free from pain, has not interfered with the success of the induction, and has not affected the vital statistics unfavorably

In the entire 750 induced cases there was no instance of abruptio placentae or of fetal death due to cerebral injury or birth injury. There was one instance of prolapsed cord, in a patient whose membranes ruptured spontaneously.

The study has shown a distinct advantage in favor of the unduced series. It one considers that this series seems to include most of those cases which promised trouble (the toxemias large babics contracted pelvic outlets apprehensive and nervous patients, etc.), the maternal morbidity and fetal mortality were surprisingly low in fact, it appears that the induction of labor saved much maternal morbidity and several fetal lives.

Breech Delivery

Local Anesthesia—M. P. Urnes and H. J. Timerman²² discuss the advantages of local anesthesia for breech. The patient is awake and able to co-operate to deliver her baby spontaneously. The uterine contractions are not affected. The relaxation of the pelvic floor and perineum obtained is comparable only to that with surgical ether anesthesia, and the excruciating pain attendant on the distention of the pelvic floor and perineum is completely obliterated. Episiotomy and forceps to the aftercoming

head (except high forceps) can be performed easily with little discomfort to the patient. The duration of the anesthesia is about one hour and a half

With the patient in an exaggerated lithotomy position, intradermal wheals are made bilaterally half way between the rectum and the tuberosity of the ischium One per cent procaine hydrochloride with 2 minims (012 cc) or epinephrine (1 1000) per ounce (30 cc) is used. The index finger of the left hand inserted into the rectum palpates the left ischial spine A 10 cm needle is passed horizontally through the cutaneous wheal directly to the spine and then allowed to slip just under and beyond it Because of the direction of the needle and the guiding finger in the rectum there is no danger of piercing the rectum From 10 to 15 cc of solution is deposited at this point, blocking the internal pudic nerve as it passes dorsal to the spine of the ischium just before entering Mcock's canal needle is then withdrawn until it lies just beneath the skin. The direction is changed laterally toward the tuberosity of the ischium, and the needle is inserted until the point strikes the bone Five cc is injected while the needle is gradually being withdrawn. This anesthetizes the large perineal branch of the posterior cutaneous femoris. Again the needle is withdrawn until it lies just under the skin, and its direction is changed vertically upward. While it is advancing, 5 cc is deposited in the subcutaneous tissue of the labium majus, blocking off the perineal fibers of the ilio-inguinal nerve The procedure is repeated on the opposite side, the operator using the same finger in the rectum or changing to the index finger of the right hand The vaginal mucosa and the skin of the perineal area as high as the clitoris become anesthetized within five minutes

Relaxation of the levator ani and the perineal muscles is usually complete

Should an indication arise necessitating breech extraction, parasacral block anesthesia is induced. The anterior sacral nerves are blocked as they leave the anterior sacral foramina The uterine contractions are obliterated, and sufficient relaxation of the uterus is obtained for the extraction to be performed. As with pudendal block, the pelvic floor and permeum are relaxed and complete cutaneous anesthesia results in practically Twenty breech extractions were performed by this method, with two fetal deaths in 18 viable cases, a fetal mortality of 11 per cent

Contraindications to the use of local anesthesia for extractions, or even for the simpler operations, are threatened rupture of the uterus, severe fetal asphyxia and inflammatory lesions of the perineum. In the cases presenting one of these objections and in the early cases previously mentioned ether was used. In six cases the parasacial block was supplemented by ether anesthesia because in the operator's judgment not enough relaxation of the uterus was obtained for him to proceed with safety

The fetal mortality of this series of breech deliveries in homes compares tavorably with that in reports of recent hospital series

Parasacial anesthesia for breech extractions in the authors' opinion is preferable to ether anesthesia, since in this series the fetal mortality was slightly lower and the incidence of maternal complications definitely lower when it was used. It possesses the added advantage that its use does not require the presence of a skilled anesthetist in addition to the operator, and it may be used in cases of toxemia or pulmonary complications.

Pudendal block anesthesia a particularly adapted to spontaneous delivery with episiotomy and forceps to the aftercoming head. It produces no relaxation of the uterus, so that the serious complications of postpartum hemorrhage and manual removal of the placenta will not occur as frequently as with the use of ether

Cesarean Section

A plea for the employment of the low cervical operation of cesarean section is advanced by D L Smith ²³ From November 1, 1927, to November 1, 1928, in Indianapolis hospitals, the maternal mortality accompanying cesarean sections was 11 3 per cent

In 1934 the mortality rate fell to 48 per cent. The rate for the classic technic was 51 per cent and for the low cervical it was 43 per cent.

In 1935 in the same four Indianapolis hospitals the maternal mortality decreased to 3.2 per cent, the rate for the classic operation being 3.9 per cent, while that for the low cervical was 1.8 per cent

Data are presented representing the cesarean section practice, preference and technic of 153 members of the Central States Association of Obstetricians and Conecologists

Sixty-three of these members reported 5393 cesarean sections with a maternal mortality of 1.4 per cent and a fetal mortality of 2.52 per cent

Of these 5393 operations, 1504 were classic cesarean sections with a maternal mortality of 2.85 pci cent, and 3889 were low cervical cesarean sections with a maternal mortality of 0.84 per cent

It is apparent from this study that the low cervical section is the operation of choice

According to F W Lynch²⁴ mortality studies concerning cesarean section attract one's attention because the

operation recently has become a common instead of a most uncommon method of operative delivery and because more than one-half of the deaths following cesarean section have occurred in women who previously had borne children through the normal birth passages Moreover, the incidence of cesarean section according to these mortality studies has risen from 11 per cent in 1927 to 33 per cent in 1934 Thus cesarean section preceded 11 per cent of all puerperal deaths in or after the seventh month of pregnancy in the report of these 15 states for 1927 and 1928 This tremendously increased incidence of cesarean section should have reduced the maternal mortality rate in the United States if the indications for the operation were sound and the mortality rate was The national maternal properly low mortality rate, however, has remained virtually unchanged for many years. This tremendous increase in cesarean section has been initiated both by the public and by the profession—the public because of desire to escape the pain and terror of labor which it has been taught to believe is an unnecessary and unmodern thing, the profession because it feels that improvements in surgical technic must have made safe an operation the surgical mortality of which could have been considerable only in almost antediluvian time Consequently physicians without special training in obstetrics, or in gencral surgery undertake cesarean section without full consciousness of the threat that their surgery entails. Its application should be limited to those cases in which valid reasons for its use exist To achieve such consideration and consequent limitation, the American College of Surgeons should restate indications for cesarean section valid at the present time and should instruct hospitals certified by its board to permit

the operation only after consultation with one of the chief obstetricians of its senior staff

Obstetric Analgesia

Paraldehyde in combination with one of the barbiturates is superior to any other method of obstetric analgesia according to L H Douglass and F W Peyton ²⁵ The value of the oral administration of paraldehyde mixed with propylene glycol, alcohol and syrup of acacia to mask the disagreeable odor was investigated. They employed the following technic

Throughout the first stage of labor all of the patients were kept comfortable with sodium pentobarbital, 1½ to 7½ grains (097 to 0.5 Gm.), and pantopon, ½ to ½ grain (10 to 21 mg) These are necessary adjuncts in the preliminary preparation for paraldehyde Patients can usually be quieted by this method, and it is only when delivery is becoming more imminent and pain approaching intolerability that paraldehyde is resorted to

Patients always met the following criteria before the paraldehyde could be given (1) Regular contractions with a frequency of less than five minutes, (2) contractions lasting 40 seconds or more. (3) cervix thinning out and dilating to 3 or 4 cm in the multigravida and 5 to 6 cm in the primigravida, (4) the head descending well into the pelvis, and (5) delivery apparently imminent in three or four hours

A solution of 50 per cent paraldehyde 40 per cent propylene glycol, and 10 per cent alcohol (90 per cent) was made up and stored in a refrigerator as was the syrup of acacia (N F). Ten drams of the paraldehyde-glycol mixture (equivalent to five drams of paraldehyde) were briskly stirred with 20 drams of the syrup of acacia immediately before ad-

ministration. The patient was told she was to receive a syrup that would produce sleep. The nares were loosely plugged with pledgets of cotton and the patient asked to swallow the half glassful of syrup quickly. This was followed by a few swallows of water and the patient allowed to recline. The cotton was then removed from the nose

The disagreeable taste and odor of oral paraldehyde was satisfactorily disguised. Forty of the patients stated that this was an entirely new-tasting medicine and not unpleasant; the other ten complained of bitterness, sweetness, or a slight burning sensation.

The absorption time was rapid by oral administration in contrast to the rectal method. Memory fled in five to ten minutes after the preparation was swallowed. No great variations in time of absorption were noted.

Complete amnesia, the desirable objective during labor, was present in 94 per cent of the cases. The primigravidas averaged two hours and 30 minutes without memory before delivery (a maximum of seven hours and minimum of 30 minutes). The multigravidas averaged one hour and 15 minutes of amnesia prior to delivery (maximum of four hours and a minimum of 30 minutes). Malgesia even with partial amnesia was obtained earlier by the preliminary medication of all cases.

Amnesia following delivery averaged seven hours for the series

Restlessness was present to only a small degree and sideboards were used on the bed but no other special care was given

The pharmacologic actions of the newer barbituite acid compounds were investigated by C M Gruber ²⁶ All barbiturates when administered orally, rectally, intramuscularly, or intravenously produce varying stages of hyp-

nosis, narcosis, or anesthesia and even death. The effect obtained is dependent not only upon the amount of the drug administered but also upon the type of barbiturate given. In experimental animals barbital and phenobarbital produce anesthesia lasting from 7 to 13 hours, amytal two to seven hours, ortal and pentobarbital one to two hours, and evipal, thiopentobarbital and thioethamyl only 15 to 30 minutes.

One of the objectionable features of all barbiturates in obstetrics is the high percentage of cases showing extreme restlessness and maniacal symptoms. Some of these patients require restraint for delivery. Some clinicians report one-third of their patients markedly restless and one-third moderately restless.

A corresponding period of excitement before the production of anesthesia is noted in experimental animals with amytal, pentobarbital, ortal, evipal, and thiopentobarbital. In some animals evipal and thiopentobarbital do not produce narcosis but convulsions

In addition to hypnosis and anesthesia all of these drugs depress the respiratory center and death may result. Since the respiratory center is affected before the cardiovascular system, there is always a possibility of using artificial respiration and thus preventing a catastrophe

The second source of danger is the effect on the cardiovascular system. Many investigators totally ignore this fact. It should be pointed out that all of these drugs depress the heart muscle. In experimental animals the heart dilates and the contractions become weaker. All of the ordinary barbiturates depress the peripheral vagus nerve endings, and a stronger stimulus is required to inhibit the heart.

The third source of danger is that the rapid injection of any of the barbiturates

causes a sudden fall in blood pressure This fall is mainly due to cardiac injury and dilatation of the arterioles, capillaries, and venules of all the organs of the body

The change in the vascular bed is also reflected in the lungs. Acute edema of the lungs may result and upon the recovery of the animal bronchopneumonia may occur. In human beings as little as 3 grains (0.194 Gm.) of membutal may produce this effect. Skin rashes and changes in the mucous membranes of the mouth may also be noted, with toxic doses, or with therapeutic doses in individuals who are hypersensitive to these drugs.

The fourth source of danger lies in their depressant action on all smooth muscles, especially when large doses are given

The author feels that in selected cases, and if given properly, the barbiturates may be tauly safe. In the hands of many, if they are used as anesthetics in unselected cases, they will be found to be dangerous drugs both to the mother and to the unborn tetus.

Anesthesia and Analgesia

T. A. Montgomery²⁷ reports an interesting analysis of the safety and efficacy of analgesics in obstetrics and the part played by them in maternal mortality in Philadelphia.

In formulating an opinion as to the acceptability of an anesthetic or analgesic method the physician must have in mind the following points first, safety, second, the annesic, analgesic or anesthetic properties, third, effect on contractions of the uterus, fourth, advantages or disadvantages in special cases, fifth, untoward reactions and idiosyncrasy, sixth, constitutional effects; seventh, effect on the fetal respiration at birth

Ether, with or without nitrous oxideoxygen induction, was administered by inhalation to 108 of the patients who died. In one instance it was indicated as the real cause of death and in another as a possible cause

Ether appears to be still the most widely used and possibly the safest of anesthetic agents in obstetric practice. It may be employed for analgesic effect in early labor in the Gwathmey technic, as "whiffs" during the second stage, or pushed to complete anesthesia by deep inhalation. It does inhibit the activity of the uterine musculature, its free administration may stop labor pains and its long continuance predispose to relaxation and postpartum hemorrhage.

It has the advantage of simplicity of technic, ease and administration and wide margin of anesthetic safety. It is of essential value for types of delivery that require relaxation of the uterus, namely, decomposition of the breech and internal podalic version and extraction. It can produce greater relaxation than is necessary for low forceps.

Nitious oxide-oxygen anesthesia was employed 34 times. In one instance the anesthesia was badly taken (or badly given) and death was attributed to its action.

This form of anesthesia has wide usage and great value. Given by a trained anesthetist, the margin of anesthetic safety, while not as great as in the case of ether, is nevertheless ample. During the second stage of labor it may be given for short periods with each labor pain and finally pushed to deep anesthesia for delivery.

The rectal injection of an ether-oil mixture as described and advocated by Gwathmey was considered as a possible factor in death in three instances. The circumstances of the three cases were somewhat similar rather long labor,

more than ordinary bleeding during and immediately after the placental stage, a sluggishly contracting uterus, further bleeding and a gradual lapse into shock when the patient was returned to bed. All three deaths might have been avoided by more efficacious treatment of the patient as the symptoms appeared

The Gwathmey method of anesthesia, while not so popular as it was five years ago, still occupies a place of importance in the obstetric armamentarium. It, like ether anesthesia, has a wide margin of safety if the patient is watched carefully

Chloroform anesthesia was employed in three patients who died of various causes. It was assumed to play a part in the death of one patient. The South has never given up the use of chloroform, although ethylene is now being used with favor in many of the medical centers. One fact is known—the long administration of this agent will cause degeneration of the liver, and when liver damage is already existent, as in pre-eclampsia, the employment of chloroform is mexcusable.

In tour of the maternal deaths spinal anesthesia was administered. It unmistakably caused the death of two of these patients.

It is the consensus of enlightened medical opinion that spinal anesthesia is a dangerous anesthetic in obstetric practice. It depresses blood pressure when blood pressure is already low, it relaxes the vascular tree when the latter is already relaxed, it impairs respiration when a normal respiratory excursion and complete oxygenation of the blood are essential, it necessitates placing the woman in the recumbent position with the head dependent when already the flat level position may be productive of syncope, and it trebles the likelihood of shock when intra-abdominal tension falls with delivery of the fetus

Local anesthesia has no detrimental effect on the constitution of the patient or the mechanism of labor. It is the least depressing of all methods and should occupy a more extensive place in obstetric practice than it does at present

Because of these advantages, local anesthesia is a method peculiarly well adapted to the situation in which loss of blood, relaxation of the uterus, fall in blood pressure, irritation of the lungs or burden on the heart would be fatal For this reason its use is indicated in cesarean section for premature separation of the normally implanted placenta. cesarean section in the presence of poorly compensated heart disease, and pulmonary disease. It may also be employed to advantage in the vaginal delivery in cases complicated with heart or pulmonary conditions - morphine analgesia during labor and free infiltration of the permeum at delivery permitting of spontaneous delivery, episiotomy, immediate repair and even low forceps

In six of the 11 deaths in which pentobarbital sodium was used death was attributable to the analgesia—quite evidently in two and quite probably in the other four. In two additional instances the choice of the analgesic method, in view of the patient's pulmonary condition, seemed singularly bad

The suspected cases had these points in common there was no other factor of enough significance to account for fatality, all the patients succumbed with a peculiar type of evanosis and respiratory depression, rapid thready pulse and shock without hemorrhage that failed to react to the usual methods of treatment. In several instances, the deaths were ascribed to heart failure or to pulmonary embolism. If this was the true diagnosis, it is peculiar that so many in-

stances should have occurred in the barbituric acid group

The barbiturates are presumed to have a fairly wide margin of therapeutic safety. This is said to be the case particularly of pentobarbital sodium. There seems, however, to be a wide range of susceptibility to the action of the drug

For their effectiveness in labor the barbiturates depend on the capability to produce forgetfulness (amnesia) and very little on analgesic effect. Their action in the former direction is greatly enhanced by the addition of scopolamine. The patient may scream as if in great agony during the course of her labor pains but wake the morning after with no clear recollection of what has taken place.

A great disadvantage of the barbiturates is the restlessness that they produce Patients under their influence may In such a prove difficult to control confused and semistuporous state of mind, pain arising from the uterine contractions is misinterpreted and the parturient becomes confused. As the time for actual delivery approaches, the patient may become uncontrollable. Careful surgical preparation and spontaneous delivery under such encumstances is impossible. Usually the patient must be anesthetized with gas or ether and delivery consummated by low or mid forceps. The labor over and the pains dispatched, the patient falls into a deep slumber and remains almost comatose for a number of hours

The most enthusiastic users of the pentobarbital sodium-scopolamine technic acknowledge that the rate of operative intervention is thereby multiplied many times, that forceps delivery becomes essential in from 40 to 60 per cent of cases. They also emphasize that patients under the influence of pentobarbital sodium must be watched with the closest.

attention, their care individualized and precautions taken that no injuries occur during the most restless periods. For this reason the method is available for use only in the hospital and can only be a source of grief if undertaken in the home.

Considering these facts, one questions whether pentobarbital sodium-scopolamine amnesia fulfils the requirement of safety. If the patient is in constant danger of injuring or contaminating herself, if her co-operation in the course of labor is utterly lost, if the incidence of operative intervention is multiplied tenfold, if the supervision of the case is transformed from an intelligent conduct of labor into the treatment of drug confusion, one doubts that the effect is worth the reaction that it produces

In reviewing the intrapartum deaths from which these statistics were drawn, one is impressed with the fact that the accoucher seemed often so bent on getting his patient asleep or her baby delivered that he gave little thought to the outcome of his hasty procedures When the birth of the child was accomplished he was abruptly confronted with the results. The lacerations gaped, the uterus relaxed, the patient's blood began to flow The analgesic agent that gave such profound rest narcotized the baby, the material that was to bring the mother forgetfulness of her experience combined with third stage bleeding to produce obstetric shock, the anesthetic that made operative delivery convenient relaxed the uterus and caused postpartum hemorrhage The situation called for real generalship and, unless it was forthcoming, fatality followed

With these assurances in mind and with confidence in her physician, the normal patient will approach her time of delivery with equanimity, accept a

moderate and safe degree of analgesia, be comforted by the watchful attendance of her physician, and pass through her delivery in better condition than the mother who is drugged to an unconscious state and whose labor becomes a blank chapter in her life

Uterine Inertia

During the last two years, A C Bell and P Playfair²⁸ treated 23 cases of severe uterine inertia by intramuscular injections of acetylcholine. Acetylcholine appears to be a substance intimately connected with parasympathetic nerve stimulation. A patient was considered suitable for treatment when labor had lasted at least 48 hours, whether with weak pains or with colicky uterine contractions Only patients in whom pregnancy had been normal and in whom there was no evidence of disproportion were regarded as suitable for treatment All patients had previously received treatment with sedatives and attempts at stimulation with enemas, and only when such measures proved unsuccessful in advancing dilatation of the cervix was acetylcholme used The dosage used was purely empirical and therefore the The most effective amount varied method was found to be four doses of 0.2 gm of acctylcholme given intramuscularly at intervals of three hours The full dosage should be given in all cases, even though the mertia appears to have responded to treatment before the tourth dose has been given drug had no harmful effect on the maternal blood pressure the fetal heart rate, the type and frequency of contractions, the dilatation of the cervix or the general effect on the patient maternal mortality was (one) 434 per cent and the fetal mortality was (three) 13.04 per cent (two of these fetuses were dead before acetylcholine was

given) Most patients showed a slight temporary fall of blood pressure following each injection. The cervix was fully dilated within 20 hours from the initial dose of acetylcholine in 17 cases and within 30 hours in four cases. In two cases the time was longer than 30 hours. In no case did the second stage of labor last more than three hours.

Oxytocics

Ergot and Pituitrin—M E Davis²⁹ writes a timely article on the use and abuse of ergot and pituitary. In 1934, Davis, Adair, Kharasch and Legault isolated a new water soluble alkaloid which for the first time satisfactorily accounted for most of the desirable oxytocic activity known to exist in ergot. The Council on Pharmacy and Chemistry of the American Medical Association has given the name of ergonovine to this new alkaloid.

This new water soluble, crystalline ergot base, which has the formula $C_{19}H_{23}N_3O_2$, is responsible for most of the oxytocic properties of active ergot preparations

The ergot preparation in the Pharmacopeia of the United States is the fluidextract. When prepared according to official instructions it should contain most of the ergonovine present in the crude drug on which its oxytocic potency depends.

The official fluidextract, when properly prepared and stored, provides a good ergot preparation which can be taken by mouth in 30 to 60 minim (2 to 4 cc) doses two or three times daily. It occasionally provokes unpleasant reactions such as nausea and vomiting, in which case its use should be discontinued. Prolonged administration may result in the phenomenon of ergotism, which usually manifests itself in the form of a dry gangrene of the extremi-

ties. The drug should therefore not be continued beyond ten days

The new ergot base ergonovine in the form of a salt may be used orally and parenterally because of its crystalline character The malleate salt of the stable and satisfactory for base is For oral administration from therapy 02 to 04 mg can be given two or three times daily. It has an advantage over the fluidextract preparation in that it can be given intravenously in 02 mg doses for its immediate effect when this The parenteral routes of 18 desirable administration may be necessary in patients who are under anesthesia or when the oral route is contraindicated

Ergonovine does not affect pulse, blood pressure or urmary output. It is therefore particularly indicated in patients who exhibit any of the vascular-renal manifestations of the toxemias of late pregnancy. Fluid extract of ergot contains chemical constituents such as the amines, which may affect blood pressure.

It was not until 1928 that Kamm and his co-workers succeeded in separating posterior pituitary into two fractions, one containing the oxytocic principle pitocin, and the second the diuretic and pressor principle pitressin

Solution of posterior pituitary U.S.P. contains both principles and is the most commonly used pituitary preparation in obstetrics. It is standardized as to oxytocic activity. The oxytocic standard is such that each cubic centimeter contains not less than eight and not more than 12 international units. The international unit, as adopted by the League of Nations, is the amount of oxytocic activity obtained by 0.5 mg of an international standard powder.

Dieckmann and Michel noted that parenteral injections of extracts of the posterior lobe of the pituitary were fol-

lowed by a marked decrease in the volume of urine, an increase in the chloride concentration, and an average rise in the systolic pressure of 51 mm of mercury pressure in a group of patients with preclamptic toxemia studied during pregnancy. Less marked changes were noted in normal gestation. In addition to warning of the inadvisability of using solution of posterior pituitary as an oxytocic drug in patients exhibiting evidences of toxemia, these authors suggest that the changes induced by the drug may be of some diagnostic and prognostic value in the management of these cases

Indications for Oxytocic Drugs—Nonpregnant Patients—Although solution of posterior pituitary will cause some contractions and tonicity of the uterus of the nonpregnant person, it is rarely indicated. The pathologic cause for the bleeding should be determined and treated

Therapeutic Abortion — Oxytocic drugs will not terminate a normal gestation in the first trimester of pregnancy. The uterus is not responsive to ergot and pituitary during this period. Experimental evidence would indicate that the corpus luteum of pregnancy inhibits uterine response to posterior pituitary extracts. As term approaches the uterus becomes more and more susceptible to the action of this substance. Near term one can cause the uterus to contract vigorously after the administration of the drug.

Ergot and pituitary, however, may be used to hasten or to complete the process once it has begun. In inevitable and incomplete abortions solution of posterior pituitary can be used in 0.5 to 1 cc doses intramuscularly with benefit to the patient.

Induction of Labor—The medicinal induction of labor is rarely successful until term is approached. This is prob-

ably due to a lack of sensitivity on the part of the uterine musculature to oxytocic stimuli If, therefore, it is necessarv to induce labor for some complication prior to term, one usually has to resort to mechanical means The method of medicinal induction of labor at or near term at the Chicago Lying-in Hospital consists of the following procedure: Castor oil, $1\frac{1}{2}$ ounces (42 cc), is given early in the morning, followed two hours later by quinine in 3-grain (02 Gm) doses at hourly or half hourly intervals for four or five doses, followed by graduated doses of solution of posterior pituitary, beginning with half a minim (0.03 cc) and increasing half a minim at each dose 15 minutes apart until 3 minims (002 cc) is given. The latter dose can be repeated until a total of 1 cc is used The uterus should be carefully observed. and if it exhibits tetanic contractions so that the fetal heart tones are interfered with, solution of posterior pituitary is discontinued. In the rare event that the continued tonic state of the uterus so seriously interferes with the uteroplacental circulation that the fetal heart rate 18 dangerously slowed, it may be necessary to administer ether to the patient for several minutes to relax the uterus

Labor—The oxytocic drugs are almost never indicated during the first and second stages of labor. It is dangerous to interfere with the normal uterine motility. Solution of posterior pituitary given during the course of labor initiates a marked tetany of the uterus. This abnormal uterine action may result in an interference with placental circulation resulting in fetal asphysia and even death

Rarely is it advisable to give solution of posterior pituitary. If this is done, the dosage should be limited to one or two minims subcutaneously. Solution of posterior pituitary and ergot find their greatest usefulness in the third stage of

labor Used judiciously and with the proper indications, the oxytocic drugs may often prevent the occurrence of postpartum hemorrhage and the serious results that may be caused by it.

In the normal conduct of the third stage of labor it is usually advisable to await the complete separation of the placenta, after which its expulsion can be aided Immediately after the birth of the placenta, 1 cc of solution of posterior pituitary can be given intramuscularly. In the event that the patient has had no anesthetic, fluidextract of ergot can be given by mouth or ergonovine can be given parenterally

Puerperium — The use of oxytocic drugs in the puerperium has enjoyed almost universal popularity Ergot has been the therapeutic bulwark for this period. It has been credited with hastening normal involution, decreasing the likelihood of late postpartum bleeding, limiting the probable spread of intrauterine infection if present and helping to maintain the genital organs in the best state possible.

Recent years have seen the introduction of a number of oxytocic preparations in which posterior pituitary is combined with some form of thymus gland extract This combination was heralded as the ideal oxytocic for labor, resulting in an increase in the effectiveness of the uterine contractions without the inherent tonicity and unbridled ac-Thus, they are supposed to speed up labor along its normal physiologic course. These preparations represent pituitary solutions diluted with mactive thymus gland substance, retaining all the undesirable and dangerous action of pituitary

Asphyxia Neonatorum

R A Wilson, M A Torrey and K S Johnson³⁰ discuss the treatment

of asphyxia neonatorum and claim it has not kept pace with other advances in obstetrics Less than five per cent of the volume of oxygen in the blood of the umbilical vein is accompanied by clinical evidence of asphyxia A brief fall below one per cent of its volume is not necessarily fatal, but longer exposures cause permanent damage to the delicate nerve cells of the center and resuscitation is no longer possible New evidence is presented indicating that the atelectatic lung cannot be opened by gases under pressure in the trachea Pressures as high as 18 mm of mercury fail to open alveoli and result in damage to the lung tissue Lower, and therefore safer, pressures are even less efficacious Morphine alone or in combination has other purposes during labor besides the relief of pain Because of this it should be administered expertly not less than two hours before delivery method of resuscitation is entirely satisfactory. In severe cases of asphyxia and respiratory depression the injection of a respiratory stimulant is logical and to a large extent the only possible way of producing a respiratory gasp. An improved technic for the administration of respiratory and cardiac stimulants, saline solutions and so on by means of the umbilical vein is described

Infant Mortality

While there has been a reduction in the number of deaths in infants under one year of age the greater part of this reduction has been in infants past 14 days of age. H. M. Bundesen, W. I. Fishbein, O. A. Dahms and E. L. Potter discuss the factors responsible for failure to reduce the death rate of infants under seven days of age. Before procedures can be effectively carved out to reduce the number of deaths in the neonatal period, the accurate causes of

these deaths by autopsies must be determined.

To determine the importance of necropsies, the eight leading causes of death found in the 608 infants dying under 15 days of age on whom necropsies were not performed are compared with those found in the 398 infants on whom satisfactory necropsies were done. In the group with no necropsies prematurity is the leading course (41 per cent)

Atelectasis is second on the list of causes without necropsies. It is stated as the cause of death in 147 per cent of this group. As atelectasis is a secondary lesion, it was not accepted as a cause of death in the series with necropsies

Cerebral hemorrhage is third on the list of causes without necropsies. It is found twice as often in the group with necropsies as in the group without

Congenital malformations is the fourth cause in the group with no necropsies, and the second cause in the group with necropsies

Asphyxia is fifth on the list without necropsies. It is stated to be the cause of death more than twice as often in this group as in the group with necropsies. On the other hand, pneumonia (all types) is sixth on the list and is stated to be the cause of death only one-third as often in the group with no necropsies as in the group with necropsies.

This indicates the difficulty of diagnosing pneumonia clinically in the neonatal period. Furthermore, even when making the diagnosis by necropsy a microscopic examination of the lung tissue must be included, since on gross examination the pneumonia may be missed or may occasionally be erroneously diagnosed. It is frequently impossible to tell the difference grossly between the lung partially atelectatic and

engorged with blood and the lung with pneumonia

Injury at birth other than cerebral hemorrhage is stated as a cause in the group with no necropsies, while it does not appear in the eight leading causes in the other group. On the other hand, edema of the brain appears among the first eight causes of death in the group with necropsies and is not found in the group without them

This comparison between the eight leading causes of neonatal deaths, as determined by necropsies, and the causes as stated without necropsy shows that there is a difference in the relative frequency and importance of the various causes of neonatal deaths, and indicates the importance of post-mortem examinations in determining the correct cause

A study of the clinical investigations of neonatal deaths and the obstetric histories showed that there were four main factors which contributed greatly to these infant deaths (1) Maternal complications, (2) inexpert obstetric care, (3) incorrect or inadequate neonatal care, and (4) prematurity

Maternal Complications—Complications in the mother were associated with 385 of the 1123 infant deaths occurring during the neonatal period. The most common of these complications, in the order of their frequency, were toxenia, placenta praevia, accidents and injuries, abruptio placentae, syphilis and hypertension. All these complications, and particularly toxenia, might be factors in the production of infant deaths.

The early diagnosis and treatment of maternal complications, therefore, are important in the reduction of neonatal deaths. In the presence of pathologic conditions in the mother, adequate antepartum care is essential.

Inexpert Obstetric Care—Inexpert obstetric care is found to be associated

with a number of the deaths that occurred from cerebral hemorrhage. Cerebral hemorrhage was the leading cause of death in the infants on whom necropsies were performed.

Attempts to speed up delivery by the indiscriminate use of oxytocics, such as solution of posterior pituitary, the unindicated application and improper use of forceps and the unnecessary performances of version and extraction, were often followed by the death of the infant

The use of analgesics, such as morphine, scopolamine and the barbiturates, during labor, adds to the hazards which many new-born infants face. With prematurity cerebral hemorrhage or the effects of prolonged labor, the additional depression of the respiratory center by the analgesic materially increases the difficulty in establishing respiration.

Prematurity—This premature infant whose tissues have not developed sufficiently to function normally will not survive unless given special care. Some premature infants have such inadequately functioning tissue, particularly in the lungs, that they will not survive under any conditions. Immediate provision for the maintenance of normal body temperature, proper feeding, particularly the use of breast milk, protection against infection, and the use of oxygen are the four main safeguards for the premature infant.

Adequate care for premature infants should be provided to bring about further reductions in neonatal mortality

Incorrect or Inadequate Neonatar Care—An essential part of correct neonatal care is the use of proper methods of resuscitation in reviving the asphysiated infant. Investigations revealed that measures often are employed which are damaging to the infant, particularly those who are prematurely born. It is generally agreed that violent methods, such

as slapping, swinging, hot and cold baths and ether sprays, are more liable to result badly than favorably

On the other hand, the skilled use of the tracheal catheter is generally accepted as the best means of clearing the respiratory passages and initiating respiration. However, it was by no means employed as often as indicated

Education in the proper methods of resuscitation is important to help in further reducing neonatal mortality

Since a series of satisfactory necropsies reveals that the leading cause of death is cerebral hemorrhage and that prematurity is a large factor in the production of many deaths, directly or indirectly, it is the authors' feeling that the chief attack in reducing neonatal mortality should be centered on these two conditions

The toxemias of pregnancy, which often result not only in premature delivery, both spontaneous and induced, but also in damage to the infant, are other factors contributing to infant deaths which need further investigation. However, the principal and most hopeful field of endeavor at the present time is to make certain that the infant is in skilled hands. The statement has been made that every mother is entitled to skilled care during delivery. The authors add that the infant, too, is entitled to the same consideration.

Therapeutic Abortion

In 1935 Borro advocated the use of formaldehyde for the interruption of pregnancy. He claimed that this substance causes the death of the fetus but also its retention for some time, making it possible for the patient to continue the treatment of the disease for which the pregnancy was interrupted. C. Masson³² made experiments on animals before he attempted to try formaldehyde.

injections in pregnant women. He chose rabbits and guinea pigs because these animals have a uterus bicornis, which often allowed him to experiment on either half of the pregnant uterus. The results obtained led him to attempt the experiment in pregnant women

After emptying the bladder, he inserted a fine needle about two inches above the pubic bone directly into the The amniotic fluid amniotic cavity flowed drop by drop into the syringe and could be used later for examination He injected 125 cc of solution of formaldehyde The patient experienced some pain in the lower part of the abdomen, but this soon subsided The pain recurred the next day and again after 48 hours with some intensity. In the first case the nurse prematurely opened the amniotic sac and about 15 minutes later the dead fetus was expelled, followed by the placenta. In all the treated cases, pain and swelling of the breasts developed three days later The quantity of formaldehyde injected may be larger or smaller than 125 cc of the 40 per cent solution, depending on the gravity of the patient's condition. In one case 0.5 cc of solution of formaldehyde did not kill the fetus but arrested temporarily the patient's toxemia, and expulsion of a live fetus took place 63 days later. In another similar case a second injection of 2 cc of solution of formaldehyde was necessary nine days later. preceded by extraction of 100 cc of ammotic fluid Six days later the dead fetus was expelled by normal uterine contractions

Calcium and Viosterol During Pregnancy

W Brehm; agrees that *calcium* is essentially necessary in pregnancy, but there seems to be some factor or factors when *viosterol* is used with it which

render it either more assimilable, its retention and deposition more pronounced. or which produce an irregular mobilization, regardless of whether the calcium is given as inorganic adjuncts or by its ingestion in foods. During the last ten years he has given to his obstetric patients, except when contraindicated, five drops of viosterol (03 cc) three times a day for two weeks and then 5 grains (03 Gm) of calcium three times a day for two weeks, alternating thus every two weeks throughout the pregnancy Soon he began to notice calcified areas in the placentas and a decrease in the size of the fontanels with fusion of the cranial sutures, which could be shown by the roentgenogram before delivery. This was easily demonstrated after delivery with a consequent lessened moulding of the fetal head and an increase in the length of labors. Marked calcification was found in the kidneys of three stillborn infants without any other apparent etiology. The author then began the study of 540 obstetric cases divided equally as follows (1) Those receiving calcium and viosterol, (2) those receiving calcium alone, (3) those receiving none of the foregoing except as turnished by a normal He found that viosterol causes diet definite calcification in the placenta. which is greatly increased by the ingestion of calcium. Cod-liver oil seems preferable to viosterol Natural vitamins when indicated seem preferable to synthetic ones. It is just as important in treating a patient not to produce by overtreatment a more serious condition than the condition originally treated

CHEMICAL DIAGNOSIS OF EARLY PREGNANCY

The test that J Patterson ¹⁴ described requires at least 50 cc of early morning concentrated urine. The urine is tested

for high acidity by treating a few drops of it with methyl red, and if acid to this indicator it is adjusted with alkali until it is no longer pink. A 50 cc sample is then heavily inoculated with bacillus coli and incubated overnight. After incubation, while it is still warm, 0.5 Gm of sodium bisulfite is added. The specimen is shaken until the solid has dissolved completely and then it is allowed to stand for 15 minutes. The partially decolorized urine is transferred to a 150 cc. separatory funnel and extracted with two lots of 40 cc of ether combined ether extracts are washed with a little water and then well shaken with a 30 cc portion of ten per cent sodium carbonate The alkalı layer having been discarded, this washing process is repeated until the carbonate layer is com-The ethereal solution pletely colorless is then again washed with distilled water. and when the laver of water has been drawn off the laver of ether is further extracted with two lots of 40 cc of tenth normal sodium hydroxide. After separation and rejection of the upper ethereal solution the combined alkali portions containing the theelol are treated with 25 per cent sulturic acid drop by drop until acid to congo red paper acidified aqueous solution is then extracted with two portions of 40 cc of pure 'analytic" ether, after which the layers of ether are combined and washed with a little water. The ether extract is given another washing with ten per cent sodium carbonate, and after the rejection of the alkali the remaining ether is freed from all trace of the alkaline carbonate by two more washings with distilled water. The final solution is transferred in two portions to a 50 cc transparent silica flask and the solvent is completely evaporated by immersing the flask in a large beaker of water previously heated to 140 to 158° F (60 to

70° C.); the last traces of moisture are removed in vacuum by direct application of suction to the flask The reagent used for the development of the color reaction of the dry residue consists of 36 parts of pure phenol with 56 parts of pure concentrated sulfuric acid (Cohen and Marrian) To obtain the color reaction 1 cc of reagent is added from the buret to the dry residue and the flask is immersed in a large water bath previously heated to about 158° F (70° C.) By frequently rotating the flask the whole of the residue distributed round the sides is brought into the reagent, and the temperature of the bath is rapidly raised to boiling point and kept there for ten minutes It is now cooled by holding the flask under a stream of tap water While this cooling process is going on 1 cc of five per cent sulfuric acid is added slowly, the contents of the flask are kept moving in order to bring the somewhat syrupy reagent into a homogeneous solution with the dilute acid. The product, which is still yellowish is then reheated in the boiling water bath for two and a half minutes A positive reaction is obtained when the original color gradually changes over a pink or red, a negative when this change is entirely absent Urines from 65 cases in which a pregnancy diagnosis was required have been examined by the test. In all except one case the result was in agreement with that of the Friedman reaction

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ORTHOPEDICS

By John Royal Moore, AB, MD, and J. T Nicholson, MD.

BACK PAIN

The Compensatory Aspects of Low-Back Conditions

Howard L. Prince1 reviewed the compensation aspects of low-back conditions "It is upon the first medical man who sees the injured back that much of the responsibility for the after-results falls I believe that all of these backs should Frightening the individual be rested or fixing in his mind the idea that he has a serious back injury should be meticulously avoided Strapping the back and urging the patient to return to work as soon as possible are, I believe, the causes of much of our difficulty in later cases, in spite of the statement of the head of one of the insurance companies that he is impressed by the better results that osteopaths obtain because they minimize the condition and do not frighten the injured man into feeling that he has a serious lesion Strapping and a few days' rest on a hard bed with the application of a little local heat-perhaps relaxing the patient completely with morphine for the first 48 hours-will enable the patient to get back to work when he feels that he can He has a feeling of having been well cared for and his inclination is to return to work The psychological character of the individual, as well as his physical condition, should be taken into consideration in every case. If the injury has occurred to a spine already showing the ravages of hypertrophic arthritis, due consideration to that fact must be given In compensation cases I am continually struck by the importance of keeping the attitude of the patient right The doctor may not be able to do this,

fancied injustices on the part of the employer may make it very difficult

"The application of casts and the use of braces, I believe, are fraught with peril Certainly before employing either form of treatment, one should be very sure that the advantage to be gained will outweigh the possible harmful effects on the patient. It is always well to look back and realize that casts and braces, which were believed in so thoroughly by the older generation, have, in most instances, failed to accomplish what they were supposed to have done I often think of the situation in regard to scoliosis,-men wrote books on the treatment and cure of scoliosis, illustrating plaster jackets and braces that pressed here and pulled there but, on final investigation, no case of cure was shown

"When it comes to question of the need or the advantage of surgery in low-back conditions, we should deliberate most carefully, because, if we give certain types of individuals a scare, they will never get out of the compensation class"

Low-Back Pain and Sciatica

A Gurney Kımberley² reported the causal factors producing low-back pain and sciatica as anatomical variations in the posterior articulations of the lumbar vertebrae, posterior displacement of the fifth lumbar vertebra, transitional lumbar vertebrae, exaggerated lumbosacral angle, spondylolisthesis and degenerative changes in the lumbar spine The articulations of the lumbar spine were normally in the sagittal plane. In the lumbosacral articulations the plane was sagit-The latter permitted tal or coronal lateral motion and rotation in addition to flexion and extension which caused instability Brailsford found in 3000 x-ray

films that 57 per cent of the lumbosacral articulations were in the coronal plane and 12 per cent asymmetrical. The asymmetry resulted in concentric motion on one side by motion produced in the other

Posterior displacement of the fifth lumbar on the sacrum was recognized by Ferguson in 1924. It was demonstrated in 203 per cent of the roent-genograms in 1157 consecutive patients treated for low-back pain. This was believed a developmental condition as it only occurred when there was atrophy of the intervertebral disc. At operation the posterior articulations were subluxated and osteoarthritic changes were found.

Transitional lumbar vertebra, Brailsford found with a partial or complete sacralization of the fifth lumbar vertebrae in eight per cent of 3000 routine roent-genograms. Spina bifida occulta was often associated with this condition Kimberly found no relationship between the side of sacralization and the side of referred pain in the 125 cases studied. The average lumbosacral angle was 43°

At a greater angle the center of weight bearing was anterior to the lumbosacral junction and produced strain upon it. It was found at operation that there was a deepening of the posterior articular fossae of the sacrum with the inferior facets of the fifth lumbar luxated into them. Sanforth and Wilson demonstrated this on a cadaver as producing a narrowed lumbosacral foramen. Ferguson further showed by lateral roentgen films of this area, taken in flexion and extension, that the posterior part of the disc was narrowed.

Spondylolisthesis occurred in 104 cases The anterior displacement of the vertebra was due to gradual stretching of the fibrous defect in the lamina between the superior and inferior articular processes

rather than traumatic dislocation with rupture of the fibrous defect. At operation it was found that the posterior processes of the vertebra were hypermobile with an existing spina bifida occulta and attenuated ligaments

Schmorl conducted a study of 3000 routine spines. In 38 per cent of these the outstanding degenerative change was herniation of the nucleus pulposus into the spongiosa. This was accompanied by a narrowed intervertebral disc, which disturbed the relationship of the articular facets causing osteoarthritic changes in them. The diagnosis of these conditions was dependent upon the roentgenogram

The nonoperative treatment of mild cases consisted in exercises to improve body posture, restriction of activities which caused back pain, adaptation to low heeled shoes, application of local heat and massage, reduction of bed sag by placing a board between the mattress and the springs and elimination of any existing foci of infection. In the cases of moderate severity, a supportive belt, corset or brace was also required In the severe cases with acute pain, recumbency in a brace on a firm bed was necessary Adhesive traction to the legs to overcome muscle spasm and flexion contractures, with daily baking and massage and sedation were indicated Epidural injections of novocain had proved of little use Forceful. manipulation occasionally produced a dramatic cure but recurrence was probable

The operative treatment consisted of a tensor fasciae latae *fasciotomy* or a *spinal fusion* or both. The former procedure was thought to be of but temporary value. The five-year follow-up on 195 patients having a Hibb's type of spinal fixation of the lumbosacral region for the conditions described above.

proved 708 per cent well, 14 per cent improved and 133 per cent unimproved

Paul C. Williams³ pointed out that lumbosacral fusion does not cure all lowback trouble. It afforded relief from symptoms in those patients who suffered from traumatic disturbance of the lumbosacral intervertebral discs, if they did not experience segmental symptoms. In each case it was necessary to do a fasciotomy in addition to the fusion. A thorough trial of the conservative program should be attempted before surgery, as postural exercises to overcome lumbar lordosis and hip flexion contractures and a low back brace for support. It was found that without these measures, the postoperative cases developed symptoms above the graft a few months after becoming ambulatory It was claimed that the conservative program eliminated the need for surgery in most of his cases

Edward L Compere⁴ reviewed 2242 cases of low-back pain Only 76 or 34 per cent were subjected to operative treatment Of these there was definite These consisted of pathology in 47 spondylolisthesis, spinal cord tumors, bone tumors, tuberculosis and chronic sclerosing osteomyelitis In the 29 others upon whom arthrodesing operations were performed, because of low-back pain with roentgenographic evidence of pathology, seven were failures, four were patients with chronic arthritis which was not recognized as progressive at time of operation, one was a compensation case, one was a psychiatric case and one died on the third day after a trisacral fusion The following conclusions were drawn Lowback fusion operations are contraindicated in infectious or multiple arthritis. compensation cases before financial settlement, elderly or poor-risk patients, female patients before puberty and any patient without definite evidence of osseous deformity or disease until con-

servative measures, including elimination of sources of infection, correction of posture, manipulations, supportive jacket or brace and division of fasciae latae have been given a trial.

Fasciotomy for Relief of Sciatic Pain

Alan DeForest Smith⁵ reviewed 49 cases in which the tensor fasciae latae had been divided (Ober's operation) for sciatic pain. All patients showed a positive Ober's sign (fixed abduction of the extended thigh when patient is lying on opposite side) prior to operation. The average post-operative observation period was 16 months. In the group having fasciotomy only 75 per cent were relieved. In the 20 cases in which lumbosacral fusion had failed to cure the sciatica, a fasciotomy permanently cured 25 per cent and temporarily others from 2 to 16 months.

Differential Diagnosis—A Steindler and J V Luck⁶ in differentiating lowback pain called attention to the structural contents of the sacral triangle, the long muscles of the back, their aponeuroses, periosteal insertions, muscle sheaths and superficial ligaments, along with the tendinous attachments of the gluteus maximus, and tensor fascia, the long posterior sacroiliac ligaments, the ligamentum sacrospinosum, the ligamentum sacrotuberosum and the piriformis majority of cases a definite point of tenderness could be located in the sacral triangle over one of these structures Cases with a contracted tensor fasciae showed a superficial midgluteal tenderness associated with a localized point lateral to the posterior superior spine Cases of sacralization exhibited a syndrome involving the deeper ligamentous structures of the sacroiliac joint, the iliolumbar ligament and transverse sacral process with pain referable to the leg

It was possible for pull on the gluteus maximus to irritate the origin point of lesions at the post sacroiliac ligament as many fibers of the gluteus maximus take their origin from the long posterior sacroiliac ligament, and in the gluteus maximus and medius at their origin from the posterior superior spine were found nerve fibers running from the posterior superior spine into the muscle. positive Ober's sign in sacroiliac disturbance was accounted for, in part, by the tensor fascia attachment by an aponeurotic fold along the gluteus maximus to the gluteal crest from which the post sacroiliac ligament arose

A diagnostic test was made from a localized point of pain to palpation or a definite spot of tenderness consistently obtained by the leg signs (Lasèque, etc.) The localized area was injected with 5 to 10 cc. of one per cent procaine hydrochloride. If the contact with the needle aggravated the local pain, elicited radiation, the procaine infiltration suppressed the local pain and radiation and the positive leg signs disappeared, the local lesion was proven. Then treatment could be conducted with reference to the offending joint, ligament or muscle attachment.

Low-Back Pain

J S Barr, A O Hampton and W J Mixter? called attention to rupture of the lumbar intervertebral disks with posterior extrusion. This caused pressure on one or more roots of the cauda equina with symptom of low-back pain or "sciatica". This could be bilateral and frequently there were remissions and exacerbations of symptoms. The patient was usually a vigorous male between 20 and 50 years. Only 80 per cent gave a history of trauma. The typical onset followed an attempt to lift a heavy object in which something gave in the low back.

The physical findings were those of a "sciatic scoliosis" Neurologic changes were absent in half of the cases. The most common neurologic finding was absence or diminution of the ankle jerk on the affected side. Sensory impairment was rarely demonstrated. A few

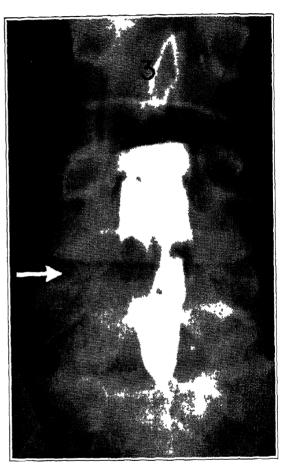


Fig 1—The rupture is unusually large and presents somewhat the appearance of an intradural tumor, but its extradural position can be readily established by roentgenograms in the lateral view. The patient is in the upright position, and there is complete filling above the lesion. Ruptured disk was found at operation. (Courtesy, Jour A. M. A., Oct. 16, 1937.)

showed complete or partial paraplegia when the lesion was so large it occluded the spinal canal

A lumbar puncture was done preferably at the lumbosacral articulation, and the first 2 to 5 cc of spinal fluid re-

moved examined for total protein content. Elevation above 40 mg per 100 cc was found in all but six cases.

The regular roentgenograms of the lumbar spine revealed no significant lesion in 50 per cent of the cases. In one-third a narrow disk was observed

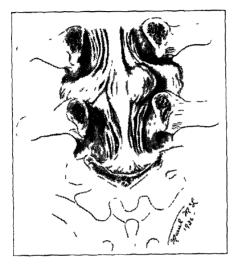


Fig 2—Schematic drawing of typical unilateral posterior rupture of the fourth lumbar disk. The laminae, pedicles and cauda equina have been removed. The nodule projects backward toward the lamina. (Courtest, Jour A. M. A., Oct. 16, 1937.)

but it was often associated with other narrowed intervertebral spaces. Roent-genoscopic examination after injecting 5 cc of iodized poppy-seed oil into the lumbar canal was necessary to establish a diagnosis.

The patient was first put in a sitting position so that the oil would settle in the sacral cul-de-sac. Then he was placed facing the roentgenoscopic table which was tilted to allow the oil to flow slowly up and down the anterior subarachnoid space. Roentgen films were made at points of obstruction. The filling defect typically appeared unilateral. Small defects did not necessarily indicate small lesions as the nodule extended laterally beyond the shadow of the oil.

The operative technic consisted in removing one or two laminae. The dural sac was retracted if the mass was on one side and opened if in midline. The iodized oil was then removed and a bone graft placed over the defect and the wound closed.

Root Pain Resulting from Intraspinal Protrusion of Intervertebral Disc

J G Love and J D Camp⁸ stressed the importance of lumbar puncture to determine the hydrodynamics of the cerebrospinal fluid. The Queckenstedt test was performed routinely to determine the presence or absence of subarachnoid block above the level of the needle. The test was usually negative but a positive

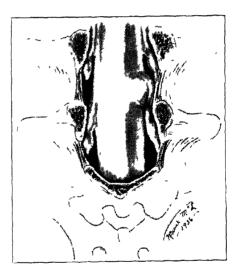


Fig 3—The cauda equina covers the nodule of the ruptured disk. It is usually more easily palpable than visualized. Note the relation of nodule to nerve root and pedicle (Courtesv, Jour A. M. A., Oct 16, 1937)

was of utmost importance. A reverse Queckenstedt test was devised to verify a disc lesion. With a spinal puncture needle in the lumbar canal, approximately 40 cc of one per cent procaine hydrochloride was injected into the caudal epidural space. In seven out of 12 cases a positive reaction was ob-

tained When a solution was injected extradurally into the sacral hiatus, the dura mater was compressed which caused further compression of an involved root producing acute pain along its distribution

The writer cautioned against indiscriminate use of iodized oil in the sub-

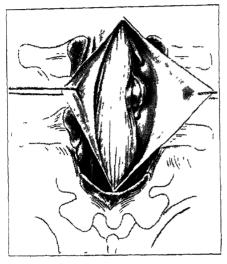


Fig 4—Appearance after opening of the dura. The relation of the intradural roots to the extradural mass is seen. Compare this illustration with the roentgenogram taken after the injection of iodized oil. (Courtesy, Jour A. M. A., Oct. 16, 1937.)

arachnoid space. He advocated it only when a definite level of motor or sensory loss could not be established by neurological examination in those cases in which conservative methods had failed and other lesions responsible for similar pain distribution eliminated. The operative procedure is a very formidable one and should be undertaken only by an experienced surgeon.

Spinal Deformity Following Tetanus. Relationship to Juvenile Kyphosis

O T Roberg, Jr, 9 reviewed 63 cases of tetanus. In all except two there was a residual dorsal kyphosis. The force initiating this deformity was explained by the contraction of certain muscle groups dur-

ing tetanic convulsions which increased the dorsal kyphosis. In 19 cases there was x-ray or autopsy evidence of fracture of one or two vertebrae. Majority of these were adults. In the 42 cases showing posttetanic kyphosis the age corresponded to that in juvenile kyphosis. The clinical and roentgenographic characteristics were similar but the level of greatest deformity was higher. There apparently was no association between the severity of the tetanic infection and the resultant deformity of the spine.

BONE

Nerve Supply of Bone

D J Hurrell¹⁰ conducted an investigation of the nerve supply of bone. Adult cat bone was used. A combination of de Castro's and Cajal's ammoniated silver method with five per cent potash alum was used. It was found that the nerves ran in or parallel to the Haversion canals from the periosteum, finally diverging from them into the matrix. The nerves entering with the nutrient vessels were destined for the marrow cavity. No part of the microscopic field in the sections examined was without nerve fibers.

Bone Atrophy and Absorption

P E McMaster¹¹ studied experimentally the influence of circulatory changes on the repair of fibular defects. Subperiosteal resections and simple osteotomies were done with aseptic operative technic in 48 healthy dogs. The results of these experiments showed a high incidence of nonunion and atrophy of the fibular fragments. "Not only did decalcification occur in the ununited fibular fragments, which was evidenced by a definite decrease in roentgenographic density, but actual absorption of the frag-

| Procedure | Infected, | Healed | Nonunion | Total |
|--|------------------|------------------|-------------|-------------------|
| Unilateral lumbar sympathectomy Unilateral femoral vein ligation Unilateral femoral artery ligation Unilateral sciatic nerve section | 7 0 0 0 | 6 2 2 3 | 6 3 0 | 19 5 2 3 |
| | 7 | 13 | 9 | 29 |

TABLE 1 BILATERAL FIBULAR SEGMENTS RESECTED

TABLE 2 BILATERAL FIBULAR OSTEOTOMIES

| Procedure | Infected | Healed | Nonumon | Total |
|---|----------|--------|---------|---------|
| Unilateral lumbar sympathectomies Unilateral femoral vein ligation | 4 1 | 6 7 | 0 | 10 9 |
| | 5 | 13 | 1 | 19 |

ment ends as well as concentric absorption of the fragment shafts, was noted" Twelve of the 48 dogs developed infections of the operative wound In 22 of the remaining 36, fibular fragments were resected from the upper third of Unilateral lumbar symboth fibulae pathectomy was performed on 12 of these 22 dogs Five had unilateral ligation of the femoral vein in the proximal portion of the thigh, while two had unilateral arterial ligations in the same location In the three, the sciatic nerve was severed in the proximal part of the The following tables show the results of these experiments

In the presence of nonunion of short fibular defects as associated conical bone, atrophy in the fragment ends was in some cases extreme. The bone was removed by lacunar absorption which was produced by giant-cell osteoclasts, and by absorption through mononuclear cells. The atrophy was explained on the basis of disuse caused by an interrupted bony continuity. In the bilateral cases, in which there was a circulatory change produced by lumbar sympathectomy or by vein ligation on the one side, absorption occurred practically the same

in both fibulae. Circulatory changes were believed to have no essential influence on bone atrophy or absorption

Diseases of Bone

Marble Bone Disease—G Gerstel¹² divided marble bone disease into two groups In the infantile one, the degree of disease progressed from the time of birth during the first months of life and led to an early death He believed this form began in utero The other type was sudden in onset, the first evidence being a spontaneous fracture He described the result of studies on a boy who died at three years and nine months, who during life presented clinical aspects of marble bone disease with anemia. He emphasized that a disease of the bone in this formative tissue should be differentiated from disease involving the bone marrow and from that of the endosteum The origin and function of bone and bone marrow were entirely different. In some species of animals the bones did not contain marrow and hemopolesis took place in special glands The endosteum which separated true bone tissue from bone marrow was capable of rebuilding the bone. Bone combined a triad of

tissues: (1) Static apparatus or true bone tissue, (2) separating and transforming endosteum; and (3) bone marrow The author on basis of microscopic and chemical studies denied that so-called marble bones were bones. He believed that small areas of true bone developed but they were insignificant in comparison with the marble masses The marble mass consisted of two parts which differed in origin and remained separate (1) Continuation of cartilaginous matrix, and (2) the filling substance. The essential disturbance was during the course of ossification in which toothlike protections of unused cartilaginous matrix occurred in the diaphyses These projections prevented the formation of trabeculae so that the primary bone became conglobated and grew as filling mass down into the diaphyses Primary bone marrow was found at the border of the epidiaphysis where there was no endosteum, that is no cells which effect rebuilding of the primary bone and decomposition of the cartilaginous matrix occurred at the site Macroscopically the outer surface of all bones presented brownish deposits which in their microscopic aspects resembled brown tumors and in this rebuilding of bones took place The periosteum was not involved in the process

Osteoporosis Melolytica (Multiple Spontaneous Idiopathic Symmetrical Fractures)—J C Leedham-Green and F C Golding¹³ described a case presenting a condition which they termed "Multiple Spontaneous Idiopathic Symmetrical Fractures" This was a 24-year-old unmarried woman who had no injuries or illnesses. Her complaint was pain on rising from a sitting position and insecurity upon walking X-ray examination showed symmetrical fractures of the ramus of both ischia and pubes and the first and second metatarsals.

There was slight demineralization of bone but no changes in blood calcium and phosphorus

Two other cases had been reported independently by Mechealis and Milkman which occurred in young adults. Neither of these cases showed changes in calcium or phosphorus and the biopsy reports, by different pathologists in each case, varied from osteomalacia to osteopsathyrosis

Osteomyelitis — W J MacNeal¹⁴ reviewed the bacteriology of bone infection and concluded that hematogenous osteomyelitis was the result of an overwhelming invasion of the blood stream by a virulent bacteria from the active suppurating focus The localization in bone depended upon diminished resistance which was associated with trauma or the growth activity at the meta-In the absence of trauma the marrow of the diaphysis was relatively resistant to infection because of the efficiency of its endothelial cells in the phagocytosis and destruction of bacteria Infection in a bone was merely one localization of a general septicemia which was the true source of the patient's illness Conservative handling, especially in children, was better than subjecting the acute cases to a radical surgical procedure

The writer advocated early use of bacteriophage intravenously and blood transfusions before attempting surgical drainage. The action of bacteriophage was not as a lytic one as occurs in a laboratory test tube but as an opsonic one favoring more effective phagocytosis. A number of cases were reported in which a phage had been used in overwhelming staphylococcic infections, such as furunculosis, carbuncles, septicemia and osteomyelitis

Osteomyelitis of the Bones of the Hand—Osteomyelitis of the bones of

the hand15 secondary to infection of the soft tissue was often treated radically by guttering or by removal of the bone Koch's extensive experience condemned such radical surgical methods. essential factors in the treatment of osteomyelitis of the bones of the hand are adequate drainage of the overlying soft parts, cleanly surgical care, and avoidance of trauma-by irritating chemicals. by addition of infection from without. and, particularly, by the use of curette and chisel If death of bone takes place a line of demarcation forms and the necrotic bone, if it is not extruded spontaneously, can be removed without trauma To attempt to determine a line of demarcation by surgical intervention too frequently results in destruction of living bone and extension of infection. and often makes recovery of the affected bone impossible"

Osteochondritis -- W P Blount¹⁶ described 13 new cases and 15 from the literature illustrating osteochondrosis deformans tibiae This was an osteochondrosis of the mesial side of the proximal tibial epiphysis similar to coxa plana and Medelung's deformity It resulted in a genu varus with recurvatum and internal rotation of the leg and was confused with rickets The roentgenogram established the diagnosis The deformity with sloping epiphysis and beaklike curving metaphysis appeared in the first two years or just before puberty At the latter age it was a result of trauma or infection, but could only be distinguished from the former by the history

Treatment was directed toward relief of mechanical strain on the knee until the epiphysis was closed. Then a simple osteotomy was done. If the osteotomy was done before the deformity became stationary, recurrence should be expected.

Osgood-Schlatter Disease—A study of Osgood-Schlatter disease was pre-

sented by J P. Cole 17 Forty cases were reviewed. All cases occurred in adolescence. In 19 no history of trauma or strain could be obtained He suggested the length of the patellar tendon as an etiological factor He found in a series of cases followed through five years of growth that the maximum lengthening of the patellar tendon was 3 mm and this occurred in only one case The epiphysis received its nutrition from the tendon as epiphyseal cartilage separated it from the tibial circulation The patellar tendon was increased in diameter in all cases and if opened at operation was found to be edematous In 31 nonoperated cases the average duration of symptoms was two years and three months In the operated group there was nine cases. The tibial tubercle was drilled and in some, bone splinters were introduced into the drill holes was advocated that the patellar tendon be split longitudinally to release the pressure from edema on the epiphysis Seven of the operated cases were relieved of symptoms in four to six weeks One continued with symptoms for one year The tibial tubercle became enlarged in all but five of the nonoperated group and always slightly in the operated

Ischiopubic Osteochondritis—Herbert A Durham¹⁸ stated that ischiopubic osteochondritis occurred in children between seven and eight years of age. No definite etiology could be ascribed to the condition but trauma was thought to be the most likely factor. The diagnosis was based on pain referable to the hip or groin, a limp on the affected side when walking, occasional pain which was so great as to prevent weight bearing, and muscle spasm, particularly the adductors, which limited motions of the hip joint. A moderate leukocytosis was usually present.

was tenderness along the descending ramus of the pubis, which was characteristic of all cases The roentgenogram was typical It showed a rarefaction at the junction of the ramus of the ischium and pubis with a surrounding shadow extending beyond the margins suggestive of callus. The treatment was essentially that of any osteochondritic disturbance, recumbency with sufficient traction on the affected leg to overcome the muscle spasm. This was continued until pain and muscle spasm had disappeared and the x-ray showed ossification of the ischiopubic junction condition was of clinical importance in that it might simulate hip joint disease It could also be confused with acute osteomyelitis since in both diseases there were local tenderness, increased temperature and leukocytosis A patient who was not acutely ill, had only a low grade systemic reaction, was considered an ischiopubic osteochondritis. The roentgenographic picture established the diagnosis

Paget's Disease-I M London and A R Bernheim¹⁹ found that there was an increased calcium tolerance in cases with Paget's disease The subjects reported to the hospital after a 12-hour fast, except for a small amount of chocolate which was given to avoid unpleasant hunger reactions that frequently followed the intravenous administration of calcium in the fasting subject Within ten minutes after the initial blood specimen was withdrawn a uniform test dose of 10 cc of 20 per cent calcium gluconate solution (0 186 Gm of calcium) was injected slowly during four to five minutes A first specimen of blood was withdrawn 15 minutes later and the second specimen two hours following the injection In the 17 cases of Paget's disease the calcium level remained the same as that

prior to the injection, except in five cases which had a slight upward curve

The test in 22 normal subjects resulted in a marked upward deviation from the preinjection level. This would indicate that the cases with Paget's disease have an increased affinity for calcium on the part of the bones and other tissues or a decreased affinity for calcium on the part of the blood. The former conclusion is in line with metabolic studies previously reported by other investigators showing a retention of calcium in the body by Paget's disease of the bone.

Osteogenesis Imperfecta — B L Fleming, H E Radasch and T Williams²⁰ studied phosphorus metabolism in a female child with osteogenesis im-They found that absorption and retention of phosphorus were below normal The blood serum phosphorus was uniformly low The gastric secretion contained no free hydrochloric acid and low total-acid values This was believed to be a factor in the poor absorption of phosphorus Roentgenologic and clinical evidence of improvement followed the administration of dilute hydrochloric acid and a high-protein diet The serum calcium also improved *

Brittle Bones and Blue Scleras in Five Generations—R G Hills and S McLanahan²¹ reported data concerning 51 persons in five generations which were traced to a common female ancestor with osteogenesis imperfecta. Of these, 27 had brittle bones and blue scleras. Sixty per cent were females. The fractures in these five generations were not present at birth but appeared in childhood and continued to occur until the age of

^{*}It has generally been disproved that calcium metabolism is effected in osteogenesis imperfecta. Serum phosphorus has not previously been found to be disturbed. This problem of low gastric acidity and phosphorus metabolism will bear further investigation.

puberty Deafness accompanied 57 per cent of the 51 cases From this study, it was concluded that fragile bones, blue scleras, a tendency to deafness and marked relaxation of the ligaments, constitute a real clinical entity which must be influenced by an endocrine disturbance

Tuberculosis - Pott's Disease in Adults-G. K. McKee²² compared the end results in cases of tuberculosis of the spinal column in which conservative methods of therapy were employed with those in which operative fixation was done Good clinical results were obtained in 70 per cent of the former, with late abscess formation in only four per cent, while such results were obtained in only 32 per cent of the latter, with later abscess formation in 40 per cent McKee concluded that a graft should serve as a local internal splint and should be employed only after consolidation had taken place with conservative therapy

Tuberculosis of the Knee -H Hellner²³ analyzed 87 cases of tuberculosis of the knee seen at the surgical clinic of Munster between 1925 and 1936 In 20 cases tuberculosis was thought to be present, but the condition was later proved to be nontuberculous Diagnosis was established by the clinical course, inoculation of guinea pigs or excision of No method of diagnosis was found applicable to all cases Exploratory excision of tissue did not have an unfavorable influence in any case Conservative treatment was not justified except in cases of early tuberculous hydrops, in which motion was still present and did not lead to cure Resection of the joint in cases of fungoid tuberculosis and amputation in those cases in which extensive secondary infection was present were the treatments of choice

Bone Changes in Sickle Cell Anemia—L W Diggs, H M Pulliam and J C King²⁴ concluded from a study of

30 cases of sickle cell anemia that the bone marrow was definitely involved This was confirmed from the microscopic and gross roentgenologic apeparances of the bones There were two factors which seemed to be working at adverse ends "One was hyperplasia, which increased the volume of the marrow at the expense of bone, and the other was sclerosis, which replaced the marrow and the substitute osteoid tissue or new bone" Osteoporosis was dominant in the bones which were engaged in the formation of blood cells, as the skull, ribs, vertebrae and pelvis Sclerosis was dominant in the bones in which normal hematopoieses did not occur The skull picture was most characteristic. If the patient survived, the combination of the two conflicting factors, gross anatomical derangements in the structure of the bones occurred.

Recklinghausen's Neurofibromatosis—A. Norgaard of Copenhagen²⁵ wrote on osseous changes in Recklinghausen's neurofibromatosis. He reviewed all cases reported in the literature and found kyphoscoliosis in most of them. This was contributed to bone changes, similar to those in osteomalacia. He found there could be either increase or decrease in the growth of the skeleton in the areas of neurofibromatosis.

Serum Phosphatase — Its Clinical Application in Disease of Bone—C Leslie Mitchell and Robert R Crawford²⁶ reviewed the relation of serum phosphatase to common diseases of bone When unusual amounts of abnormal bone were found the serum phosphatase was increased In Paget's disease, osteitis fibrosa cystica, osteoblastic osteogenic sarcoma and rickets increased serum phosphatase was found There was no relationship between the serum phosphatase activity and fractures In destructive bone lesions, such as osteo-

myelitis or bone and joint tuberculosis no change was noted

Studies of Longitudinal Growth of Long Bones-E L. Compere and C O Adams²⁷ conducted a number of experiments on rabbits to determine the effect of trauma to the shaft of the tibia They discovered that upon growth trauma to the shaft or to the diaphysis or metaphysis of the long bones with or without interruption of medullary blood supply did not produce any definite increase in the rate of longitudinal growth, unless it was of sufficient intensity to produce a gross fracture Such fractures involving considerable portion of the shaft and necessitating extensive repair over a long period of time did produce epiphyseal stimulation and longitudinal overgrowth This overgrowth occurred only during the time of healing The stimulation appeared to be in proportion to the amount of hyperemia and increased vascularity of bone and soft parts The longitudinal overgrowth occurred just as frequently in gross fractures in which there was no initial shortening as in those with loss of continuity of shaft and malalign-This indicated that hyperemia was a basic stimulus for growth following fractures rather than growth occurring as a compensatory phenomenon for malalignment

Bone Grafting

Svante Orell²⁸ described three types of graft which he used instead of the fresh autoplastic bone graft "Os purum" was bone obtained from the slaughter house or amputation specimens. It was freed of surrounding soft tissues, the protein was extracted by soaking in salt solution, the connective tissue by soaking in potassium hydroxide and the fat extracted by acetone. In between these processes irrigation

was carried out to free the bone canals of any debris. The "os purum" was then cut in various shapes required in application as bone grafts

"Os novum" was produced by implanting a long, narrow splint of "os purum" subperiosteally over the surface of the tibia. This was removed one or two months later at which time a profuse growth of new, soft, vascular bone had taken place in the clefts between the periosteum, "os purum" and the tibia. This new bone or "os novum" was then excised and transplanted to the desired place

Boiled fresh bone differs from the latter in that it contains fat connective tissue and proteins. It was stated that boiled dry bone when used for grafting was less satisfactory as its resorption and growth of new bone proceeded very slowly

"Os purum" was used in extra-articular tuberculous lesions to fill the cavity after its evacuation in tuberculosis of joints of foot, knee and shoulder, to fill all bone defects after resection to establish osteocynthesis and in osteoplastic cuneiform osteotomy of the lower leg. There was primary healing in all cases except one which had a sinus before operation.

"Os novum" was used for osteocynthesis of the spinous processes of the vertebrae for arthrodesis in tuberculosis of the sacroiliac joint, and repair of pseudarthrosis with uniformly good results

Boiled bone was used as a transplant in pathological conditions such as chronic osteomyelitis and osteogenic sarcoma with resection

BURSITIS

R L Patterson, Jr, and W Darrach²⁹ described the treatment of 63 cases of subdeltoid bursitis, in which the

average period of disability was 48 days The method of treatment was that of needle irrigation devised by Smith-Petersen The cases selected were based on clinical symptoms, inability to abduct or externally rotate the arm, acute localized tenderness over the region of the subacromial bursa or the supraspinatus tendon and the roentgenogram. The latter was of value in determining if the cases would respond to treatment If the film showed a dense, well rounded but bone-like shadow, irrigation was of no value In the acute cases without evidence of shadow or in those cases which the shadow in the roentgenogram was fuzzy in appearance, excellent results could be expected The technic consisted of preparing the affected shoulder with iodine and alcohol Then. with the hypodermic needle and novocain, a small wheal was made over the tender point A second point was inwith novocain about onefiltrated fourth inch posterior to the greater tuberosity of the humerus After puncturing the skin with a scalpel a large needle was introduced through the skin at the site of the first wheal and directed posteriorly and upward toward the inner surface of the acromion process At about the depth of one-half to threefourths inch, resistance of the bursa wall could be felt. As this was punctured, a cloudy fluid, at times, pushed the plunger of the syringe back

The second needle was then introduced until it encountered the superior facet of the greater tuberosity and was redirected into the direction of the position assumed by the anterior needle. The syringe was then filled with normal salt solution which was forced through one needle flowing out the other. The amount of saline used varied from 1 to 2 ounces (30 to 60 cc.) When no more material, which at times was crystalline

or even the consistency of thick cream, was obtained the needles were withdrawn. A general passive manipulation could then be done without harm and without pain to the patient. The following day the patient's arm was sore from the traumatic effect. The patient was kept in the hospital the first night with the arm held in the position of abduction and external rotation. The second day the patient was discharged from the hospital and local heat treatments and active motions were given until function of the shoulder was regained.

Painful Shoulder

L K Ferguson³⁰ studied 200 patients suffering from: (1) Acute traumatic bursitis, (2) acute bursitis with calcification, (3) subacute traumatic bursitis, (4) chronic bursitis, and (5) tendinitis or obliterative bursitis Treatment was given for each type of painful shoulder Acute traumatic bursitis was treated by immobilization of the shoulder by adhesive, application of heat and exercise after the tenth day, gradually increasing the motion until normal function was reached Calcified bursae were excised and a sling applied In subacute traumatic bursitis with calcification, conservative treatment was advocated rather than an operation Local heat was applied and the bursa injected with 20 to 30 cc of one per cent solution of procaine hydrochloride Chronic bursitis presented changes in the greater tuberosity with excrescences and small defects at the insertion of the supraspinatus tendon on the greater tuber-This type was treated conservatively and operatively If after four weeks of conservative treatment of baking and rest the pain still persisted, excision of the bursa was recommended He concluded that the prognosis for all of these types was good

R H De Orsay, P M Mecray, Jr, and L K Ferguson³¹ reported jointly a series of 50 cases of ganglion, 19 traumatic and 29 of unknown origin. These were treated by one of three methods—rupture in which they got a 50 per cent cure, aspiration, and excision Excision proved the best method since 85 per cent cure was obtained.

Tennis Elbow

Treatment-G P Mills32 reported 58 cases of tennis elbow. The chief symptom was pain when gripping an object, particularly with the arm in pronation The examination usually revealed slight limitation of extension of the elbow joint There was tenderness over the radiohumeral joint in 74 per cent of the cases and less frequently over the epicondyle in 26 per cent. The latter group presented no limitation of The treatment consisted of extension manipulation under nitious oxide anesthesia. The wrist and fingers were held in flexion with the forearm pronated Then the elbow was forced into full extension. In the cases with epicondylar pain, firm pressure was made over this site with the thumb of the hand which controlled the elbow The response to the manipulation was classified as follows

- 1 Straightening with click, 13 cases
- 2 Straightening with adhesions giving away, seven cases
- 3 Gradual straightening without click or snapping of adhesions, seven cases
- 4 Straightening without resistance, three cases
- 5 Unable to obtain straightening, one case (this was a failure)

Twenty-eight cases out of the 33 which were followed had been cured by one manipulation and two by a second manipulation *Two weeks' rest* was always advised following manipulation

An opinion was expressed that the symptom complex of tennis elbow was due to the injury of the coronary ligament. This was influenced by a case which had had an open operation in which the fragment of the coronary ligament was interposed between the radio-humeral joint.

This does not explain the presence of a calcification which frequently occurs in the x-ray film at the site of the radio-humeral bursa. It furthermore does not explain the cases which respond to free-ing the origin of the extensor carpitadialis brevis. It is our opinion that the pathology in this condition continues to remain somewhat of a mystery

MUSCLES AND TENDONS

Rupture of Muscles and Tendons

- J L De Courcy³³ claimed that tendons form the insertion of muscles to their bony attachment and any disturbance of their physiology was linked necessarily with the muscles of which they were a part. Because of the greater blood supply, ruptures in the substance of a muscle group gave rise to extensive hemorrhage. When the tear was in the tendon, signs of hemorrhage were less but the possibility of necrosis was greater. The common procedures for the repair of ruptured tendons were
 - 1 Tenorrhaphy.
 - 2 Reconstruction by lengthening (splitting), or
- 3 **Tenodesis** or implantation to a new point of attachment
- 4 Tendon grafting (transplantation)

The points of technic not to be forgotten in any operation on tendons or muscles were listed as follows

1 Never forget to look for a hematoma or to remove it, including all traumatized tissue

- 2 Do not suture a tendon under excessive tension, maintain exactly the normal amount of tension to enable the tendon to reach its place without pulling
- 3 Do not forget to dissect back widely where the tendons are extensively lacerated.
- 4 Be sure that you have done a complete debridement of the skin wound before closure.
- 5 Take great care to maintain the integrity of the vaginal ligaments of the tendon sheath
- 6 In suturing always have your alignment correct. The line of traction must be mechanically faultless
- 7. In making transplantation do not expose the tendon for one unnecessary second.
 - 8 Never wrap a tendon in gauze.
- 9 Never grasp its gliding surface with forceps
- 10 Never make violent traction upon a tendon
- 11 Be sure that the injured tendon is supplied with an abundance of well oxygenated blood
- 12 If there is much skin soiling, wait two weeks for the skin to heal before you operate Infection may ruin your result

Rupture of the Biceps

Pathology and Clinical Findings-

T Bjorkroth³⁴ maintained arthritic and periarthritic changes in the shoulder joint predisposed the biceps tendon to rupture because of its intra-articular course A series of six cases were reported with rupture of the short head and of the common tendon of the biceps Dislocation of the shoulder predisposed to rupture of the biceps From this lesion, and not from chronic arthritis, disability was caused in elderly indi-The treatment recommended viduals was to loop the tendon through a tunnel at the base of the greater tuberosity Four of the six obtained good results from this procedure

Acute Suppurative Tenosynovitis of the Flexor Tendon Sheaths of the Hand

R S Grinnell³⁵ wrote that acute suppurative tenosynovitis of the flexor tendon sheaths of the hand frequently

resulted in permanent disability because of poor treatment. A series of 125 cases was reported with an average follow-up of 16 months. Puncture wounds were the injury causing the infection. The flexor finger creases were the most frequent sites of the injury. From this, any wound at the finger crease should, therefore, be regarded as a threat to the tendon sheath. Tenosynovitis occurred most frequently in the first three fingers of the right hand Errors in diagnosis caused delay in operation in 25 per cent of the cases The end results were poor. They were classed in four groups based primarily on function Over one-third of the cases were in the poorest group Nearly two-thirds were in the lower two groups Only 17 per cent had complete or nearly complete function necrosis of the tendon occurred in 52 per cent At the time of operation streptococcus hemolyticus was present in 36 per cent of the cases and the staphylococcus in 31 per cent The best results were obtained in the thumb, and the poorest results in the fifth finger Primary tenosynovitis occurred in 54 per cent and secondary in 58 per cent of the cases The results were about the same There was one for the two groups death, three arm amputations and eight Osteomyelitis ocfinger amputations curred in 38 per cent. The average period from operation to complete healing was 53 days and twice as long as they in cases with tendon necrosis

From this study of 125 cases it was concluded that delay before operation was probably the most important cause of the poor results

Progressive Muscular Dystrophy

Y. Hırata and K Suzukı³⁶ studied the effect of vitamın C in ten patients who had marked progressive muscular

dystrophy Their tabulations reported that these patients had a C hypovitami-They decided to attempt treatnosis Patients were ment with vitamin C given daily from 200 to 500 mg by intravenous or intramuscular injection During the course of treatment the cerebral spinal fluid revealed an increase Subjective and in vitamin C content objective improvements were noticed They concluded that the oral administration of vitamin C surpassed in efficacy any other treatment of progressive muscular dystrophy It exerted an especially favorable effect on the muscular ady-No regeneration of impaired namıa muscle fibers was noted Muscular metabolism in relationship to glycogen and creatine-phosphoric acid and adenylpyro-phosphoric acid was improved

JOINTS

Experimental Joint Sprains

L J Miltner, C H Hu and H C Fang 37 used varying amounts of manual force to knee and ankle of ten rabbits to produce mild and severe strain, without x-ray evidence of fracture Trauma caused immediate inflammatory response of the muscular structures around the point of greatest strain. If the injury was severe enough to cause involvement of bone or cartilage, the healing was slower In the mild sprains gross evidence of injury disappeared the fourth Pathological evidence, however, could be found until the sixth week In the severe strains there was a similar reaction of the soft tissues and microscopic evidence persisted two to four weeks after the clinical condition was satisfactory It was concluded that joints should be rested at least two weeks after gross symptoms of injury had subsided

Joint Changes from Patellar Displacement

G A Bennett and W Bauer38 used a number of rabbits in which they sutured the patellar tendon so that it would exert a mesial pull across the joint surface This was done without entering the knee joint The displaced patella caused demonstrable changes in the joint after four weeks There was a rapid loss of underlying articular cartilage and subsequent eburnation of the subchondral bone This apparently was due to the absence of normal patellar apposition and lack of lubrication of the non-articularing surfaces by synovial fluid Following proliferation of the connective tissue at the perichondrial margins, there was a marginal over-growth sufficiently marked to form a new articulating surface for the patella The repeated stretching of the synovial membrane was thought to be sufficient stimulus to cause the perichondral connective tissue to proliferate This proliferation which normally occurs in all joints, to some degree, with increasing age and long continued use, develops much more rapidly in joints with anatomical derangements A comparison of the pathological findings was made with that of a patient who had bilateral displacement of patella and resulting degenerative joint disease They concluded that early correction of dislocated patella was indicated to prevent such joint damage

Congenital Dislocation of the Hip

Arthrography — J A Leveuf and P Bertrand³⁹ were able to demonstrate the narrowing or even closure of the articular capsule in cases of congenital dislocation of the hip by introducing 10 cc of a 30 per cent solution of colloidal thorium dioxide, neo-iopax or other

radiopaque substances into the hip joint anterior to the head of the femur. This was very helpful in determining the method of reduction. The wide separation of the head of the femur and the acetabulum indicated closure of the capsule. Thereby indicated open reduction was necessary. In 15 cases, in which this method was used, no ill effects were observed.

Auscultation of Joints

A Steindler⁴⁰ stressed the importance of auscultation in the examination of joints He presented a preliminary report based on the auscultatory findings in a series of 397 knee joints. The instruments used were the stethoscope, the cardiophone, and the oscillograph The interpretation of sound phenomena was difficult because extraneous and extra-articular noises had to be differentiated from the intra-articular noises Certain sounds, however, could be considered intra-articular because of their character and the regularity of their Sustained grating in all occurrence quadrants of the knee joint indicated general involvement of the joint with arthritic changes which could or could not be the background of isolated in-Isolated sounds ternal derangements were cracks, clicks and thuds pitched cracks indicated a hard body. such as a joint mouse, while low pitched clicks and thuds indicated softer bodies, such as fringes and semilunar cartilages No claim was made as to the ability to make a definite diagnosis by auscultation but it was believed to be of aid in locating the lesion inside the knee

Chondromatosis of the Joints

E Freund⁴¹ believed that chondromatosis of joints did not represent a blastomatous change of the synovial

membrane. This conclusion was based on clinical, roentgenological and pathological study of three cases. He believed that the process was similar to that of myositis ossificans and that the close embryonal relation of synovia to cartilage explained the prevalence of cartilaginous tissue in chondromatosis.

Hallux Valgus

A New Operation - According to G R. Girdlestone and H J. Spooner⁴² hallux valgus consisted of valgus of the proximal end of the phalanx and varus of the first metatarsal bone, with splayfoot. The more common types of operation for hallux valgus were: (1) Resection of the head of the first metatarsal bone, and (2) hemiphalangectomy, which reduced the deformity but did not improve the splayfoot or the metatarsalgia, if present These difficulties might appear postoperatively, if not present before For this reason a new operation was devised, consisting in the removal of the exostosis, removal of the cartilage from the proximal end of the phalanx and removal of all of the proximal phalanx except the very base containing the attachments of the adductor hallucis muscles This small block of bone was fastened as far medial as possible on the head of the first metatarsal bone with a beef bone peg This operation improved or prevented splayfoot as well as relieved the hallux valgus and hallux rigidus Ten of 20 patients with hallux valgus treated by subtotal phalangectomy complained of metatarsalgia and splayfoot postoperatively and three complained of them preoperatively Thirteen of 30 patients from 14 to 68 years of age, who were operated on by the new technic, had metatarsalgia preoperatively, but only one complained of it postoperatively

Extra-Articular Arthrodesis of the Hip

Simplified Technic by Means of a Tibial Graft—H. L Rocher⁴⁸ recommended a modification of Massart's type of arthrodesis of the hip typical anterior Smith-Petersen incision was made and then a longitudinal external incision was made over the greater trochanter A hole was drilled over the base of the greater trochanter, emerging at the upper surface of the neck The capsule was not opened A bed was gouged in the side of the ilium, and a tibial graft was passed through the drilled hole in the trochanter and buried in the ilium. The limb was then immobilized in plaster

Fixation of the Hip Joint with an Extra-Articular Bone Graft

Hugh C Trumble⁴⁴ reported the end results for fixation of the hip joint by means of an extra-articular bone graft. The graft was placed between the ischium and the shaft of the femur below the level of the lesser trochanter. This type of fixation was used on eight patients with tuberculosis of the hip joint. Seven had well united grafts. One fractured the graft 18 months after operation.

Spastic Paralysis

Treatment of spastic paralysis is discussed by F H Mills ⁴⁵ The lesion was caused by damaged cerebral cortex. The etiological factors were birth injury, encephalitis following acute specific fevers as diphtheria, typhoid, poliomyelitis, syphilis, infantile cerebral hemorrhage, or arrest or failure of development of cerebral cortex. A great mistake was made in judging individuals with spastic paralysis as mentally in-

ferior Over 50 per cent of the 200 cases used in this study gave the impression of being idiots because of drooling and speech difficulty (After treatment only four were rejected as true idiots)

The sensory disturbances in spastic paraplegia were not generally realized. There were (1) Loss of appreciation of relative intensity of different stimuli as heat, cold and touch; (2) loss of tactile localization, (3) tactile discrimination, (4) proproceptive impulses, and often (5) astereognosis was present

The treatment of general health with supervised diet and rest was stressed. Attendance at school was detrimental, as their awkwardness often excited jeers from classmates, the embarrassment of which provoked greater difficulty in movements. Lessons were given at home by the mother or a tutor

The first essential of the treatment was to inhibit muscular spasm. A warm bath of 986° F (37° C) was given at the start of treatment. The patient was then taught to relax and breathe deeply, the affected muscles manipulated, beginning with the more proximal group as deltoid, trapezius and pectorals When muscles could be manipulated without exciting stretch reflexes, passive motions of joints were begun These were carried out only by focusing the patient's attention of abduction, adduction, etc. This part of the treatment was most tedious and often took vears

Special exercises came later. These were mainly concerned with balance. This was obtained by stair climbing, walking in sand, etc. Last were exercises in co-ordination. These were directed for finer movements as use of tongue in speech and motions of small joints of fingers and toes.

The treatment of fixed deformities was by manipulations which were advocated at an early age. In 370 patients, tenotomy alone was necessary in but three.

Patience and conservatism cannot be stressed too strongly in these unfortunate cases In presence of fixed deformities, manipulations and tenotomies alone are seldom beneficial.

THE FOREFOOT

Structural Anomalies in Relation to Some Metatarsal Disturbances

J Bruce⁴⁶ had an interesting monograph on this subject. He described the development of the "terrestrial foot" from the aboriginal. He concluded that certain metatarsal conditions were related to the primitive foot Interesting x-ray films were shown to illustrate the various conditions which arose tarsalgia described by T. G Morton in 1876 was due to the weight bearing line being thrown through the third metatarsal head "Marching foot" reported by Bruthaupt in 1855 again originated from a lateral deviation of the weight bearing area on the forefoot Kohler's disease (Freiburg's disease) he believed was also due to the same disturbance which in turn caused multiple minor trauma to the metatarsals predisposing them to disruption of the trabeculae and resulted in repeated small hemorrhages and bone absorption and repair as evidenced by the x-ray films and pathological sections

Every endeavor should be made to protect this primitive type of foot from developing such disturbances by use of lower heels, anterior arch pads and exercises to develop toe flexor muscles and stretch the achilles tendon

AMPLITATIONS

C. L Callander⁴⁷ described an amputation in the lower third of the thigh proximal to the adductor tubercle. The advantages of this procedure were dissection through tissue planes, control of hemorrhage without tourniquet, a broad cancellous end of the femur for weight bearing, the utilization of the patellar fossa for the stump end, closure of wound with half a dozen skin sutures only and speed in which the operation was done without shock to the patient

The knee was held in 45 degrees flexion. The operator stood on the opposite side of the table facing the mesial surface A longitudinal incision was started 3 inches (76 cm) proximal to the adductor tubercle and continued distally between the sartorius and semitendonosis to the tibial tubercle incision continued proximally on the lateral side posterior to the iliotibial band to the level of its starting point on the mesial side A lower flap was made starting at the adductor tubercle and curving distally posteriorly across the midcalf. By blunt dissection between the internal hamstrings and the vastus medialis, the popliteal vessels were identified, ligated and divided. The popliteal nerve and peroneal nerves were injected with absolute alcohol. The patellar tendon was dissected free from the tibial tubercle and the patella enucleated The hamstring tendons were freed from Then the femur was sawed the tibia through just above the adductor tubercle The end of the femur was placed in the patella fossa No sutures were used for the tendons and Michel clips or silk sutures were used in the skin. There was a profuse serous drainage from the loose skin flaps for several days. The long posterior flap soon shrunk up proximal to the stump end

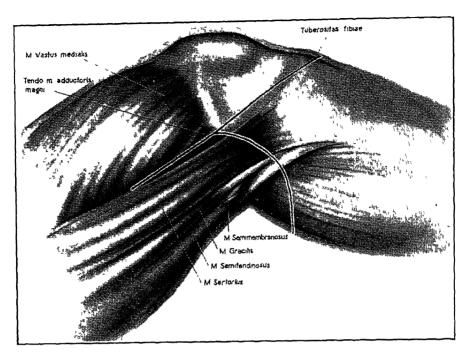


Fig 5—Medial surface of left thigh and knee Skin incisions on medial side of the low thigh and knee marking long anterior and posterior flaps. Attention is directed to the amuscular and avascular interspace between the vastus medials and sartorius muscles. Note that the flaps for this low thigh amputation are derived from the soft parts of the leg. (J. A. M. A., Nov. 30, 1935.)

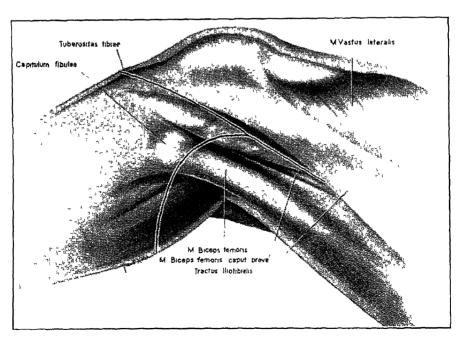


Fig 6—Lateral surface of left thigh and knee Skin incisions on lateral side of the low thigh and knee marking long anterior and posterior flaps. Attention is directed to the amuscular and avascular interspace between the tendon of the tensor fasciae latae (iliotibial tract) and the biceps muscles. The biceps muscle is composed of fleshy fibers almost down to its insertion on the head of the fibula (J A M A, Nov 30, 1935)

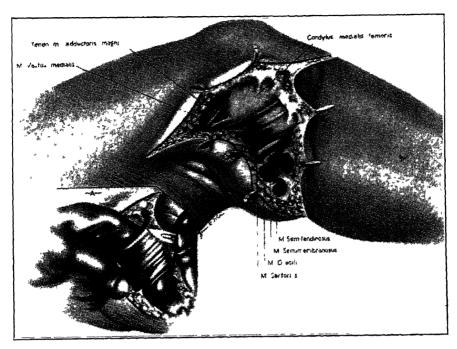


Fig 7—Medial surface of left thigh and knee Deepening the flap incisions through the deep fascia on the medial aspect of the knee to expose the medial hamstring muscles. Inset shows the bunching of the medial hamstring tendons at their insertion of the tibia, and the method of their section (J A M A, Nov. 30, 1935)

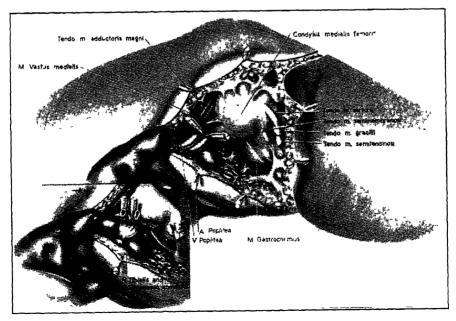


Fig 8—Medial surface of the left thigh and knee. Further deepening of the flap incisions on the medial aspect of the knee. The vessels and nerves in the popliteal space are sectioned. The main drawing shows the retraction of hamstring muscles after section at their tendinous insertions on the tibia. The contents of the popliteal space now are widely accessible and the vessels are ligated. The inset demonstrates the method of securing and dividing the tibial and common peroneal nerves. (J. A. M. A., Nov. 30, 1935.)

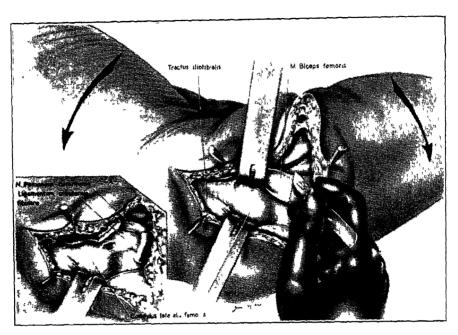


Fig 9—Lateral surface of left thigh and knee (knee rotated medially toward surgeon) Deepening of the flap incisions on the lateral aspect of the knee. Left knee forcibly rotated medially. The interval between the iliotibial tract and the biceps muscle is defined and the biceps is sectioned at its insertion on the head of the fibula. The inset indicates the structures deep to the biceps tendon. The common peroneal nerve already has been sectioned through the medial approach. (J. A. M. A., Nov. 30, 1935.)

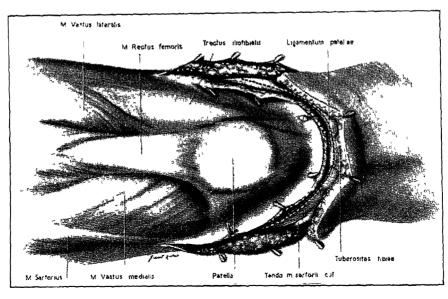


Fig 10—Anterior surface of left thigh and knee The incision marking the anterior flap is deepened through the knee joint capsule and infrapatellar tendon down to the tibia (J A M A, Nov 30, 1935)

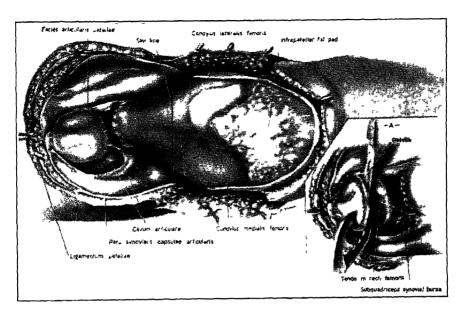


Fig 11—Anterior surface of left thigh and knee Upward dissection of the anterior flap and removal of the patella from the joint side. The saw line in the main drawing is well down into the condylar flare. The inset shows the sharp dissection of the patella from its fossa in the quadriceps tendon, leaving the rectus femoris tendon intact to act as a buffer for the cut end of the femur. (J. A. M. A., Nov. 30, 1935.)

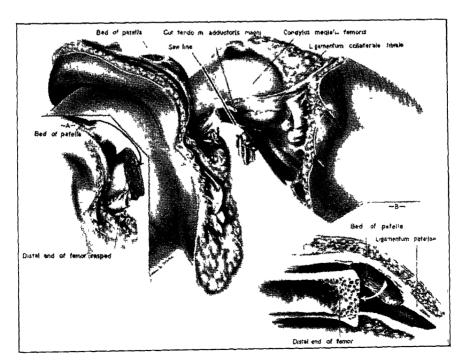


Fig 12—Medial surface of left thigh and knee Section of the femur after formation of long anterior and posterior flaps. Inset A, the patella fossa is ready to receive the cut end of the femur. Inset B shows the anterior flap loosely approximated to the posterior flap. As the flaps unite and the posterior flap retracts, the patellar fossa lodges the femur end (J A M A, Nov. 30, 1935)

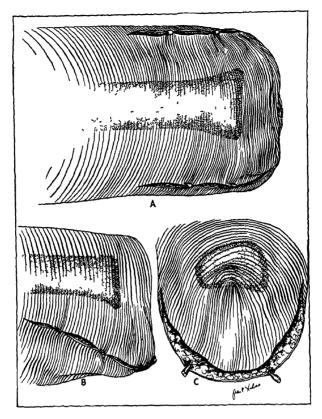


Fig 13—Transparency drawings to show the location and size of the condylar end of the femur in the redundant amputation stump A is a view of the stump from the front, B is the stump seen from the side, C is the stump viewed from the end before the clips have been placed. The skin clips are the only means of approximating the flaps at the time of operation (J A M A. Nov 30, 1935)

FRACTURES

History of Fracture Treatment Up to the Sixteenth Century

W A Clark⁴⁸ has written a very interesting article on the "History of Fracture Treatment Up to the Sixteenth Century," in which he expressed the idea that the mechanical factors in fractures were the same in the first century as they are today. The methods of treatment in ancient times were, therefore, similar in principle and practice to our methods in the present day. He reviewed the Egyptian, Greek, Roman, Arabian, French, German, Italian, English methods and those used by the American Indians "The most striking fact encoun-

tered in such a study was that many of our supposedly modern inventions and methods—some of which bear names of doctors of the nineteenth and twentieth centuries — were discovered and practiced 2000 or 3000 years ago "The gist of this excellent article can be summed in the words of J O'Donnell Bennet "Whenever I get a new idea, I look up and see which Greek author had expressed it best"

Fracture-Dislocations of the Cervical Vertebrae

W. Cone and W. G Turner⁴⁰ reviewed 36 patients with injury of the cervical vertebral column. They advocated, following neurological and physi-

cal examinations, that the attending physician accompany the patient to the x-ray room in order that he may manually immobilize the head as the roentgen facets were put in place. The lumbar manometric test (Queckenstedt) was done using a blood pressure cuff around the neck in order that the exact amount of jugular compression could be recorded Then skeletal traction was applied to the skull either by tongs or heavy rustless steel wire through small holes in the skull Reduction could later be maintained by a plaster jacket Twelve cases were treated by bone graft as it was believed that in multiple fractures, fractures of the odontoid and recurrence of deformity after careful immobilization that fusion was imperative. The age of the patients ranged from 6 to 72 years There were no mortalities

Vertebral Fractures

Fractures of the spine were reviewed by B T Edy ⁵⁰ There were 245 involving cervical, dorsal and lumbar regions. One hundred and fifty-three were fractures of the body. The fifth and sixth cervical and the first lumbar and twelfth dorsal were the most frequent sites. Fractures of the thoracic vertebrae were less frequent but had a greater incidence of cord injury. In the 72 cases with cord involvement there were 41 deaths.

K Ebhardt⁵¹ found that in a series of vertebral fractures 28 per cent had been overlooked at the time of the original injury. The neglect of the vertebral fracture gave a poor prognosis, except in young athletic individuals. Adults were generally disabled if allowed up before the fracture had healed. It was found, however, that in the unreduced fractures a short period of treatment with early mobilization gave a much better prognosis than simply prolonged rest in bed.

Fractures of the Dorsal and Lumbar Vertebrae

William Rogers⁵² again called attention to the important consideration which fractures of the vertebral column should receive. This fracture comprised over six per cent of all fractures throughout the skeleton Its reduction was important, not only to prevent altered weight bearing in the spine, but the possibility of damage to the spinal cord Correction of the vertebral body deformity had been perfected in the past few years to such a degree that the surgeon could deal with the injury confident of success The injuries of the spine were classified according to the fracture of the vertebral body, dislocation of the vertebral body, and isolated fractures of the transverse, spinous and articular processes, the laminae and pedicles A diagnosis of fracture and dislocation of the dorsal and lumbar vertebral bodies without cord injury was based on the history of accident, such as a fall in which the patient landed on his feet, buttock or upon his head, neck or shoulders, an automobile accident in which the patient was flung against the car or the ground, a dive into shallow water, the patient having struck the back of his head or neck, and a blow from a neavy object falling on the head, neck or shoulders when the spine was flexed Pain was localized in the region of the spinous processes about the fracture with or without a sense of girdle constriction This could be diffused over considerable part of the back and might be referred along part of all the corresponding peripheral nerve segments Muscle spasm was marked in the back and abdomen Angulation of the vertebral column was usually not apparent No nerve root injuries, disturbance in sensation and flaccid paralysis were found in the distribution of corresponding peripheral nerves

When the cord was damaged there was pressure or complete motor and sensory paralysis below the level of the lesson If cord lesion was partial, spasticity with increased reflexes developed

Treatment—Emergency treatment when a spine injury was suspected consisted in carefully rolling the patient face down upon a stretcher or carrier

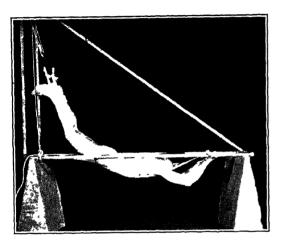


Fig 14—The suspension method of obtaining spinal hyperextension combined with traction. The patient is placed face downward upon the hammock. The lower extremities are gradually raised by means of the block and tackle. The surgeon is thus able to extend the spine gradually while the correcting forces are always under complete control. The felt padding may now be arranged about the torso and the jacket applied. (Courtesy, Amer. Jour. of. Surg., Dec., 1937.)

If paralysis was present, any hard objects should have been removed from the patient's pockets to prevent the development of pressure sores during transportation. Unless shock was present, the reduction was carried out at once A general anesthesia was never used Morphine, gr $\frac{1}{6}$ (0.01 Gm) and scopolamin, gr $\frac{1}{200}$ (0.32 mg), in two doses one hour apart were preferred Reduction was accomplished by hyperextension of the spine. This was accomplished by a number of different methods

In lieu of special equipment, the patient was placed face down on a sheet folded to a width of 8 inches (203 cm) and stretched between two tables, the head table 18 inches (4572 cm) higher than the one at the foot Gradually the tables were pushed slowly toward one another so that the folded sheet sagged between them, allowing the patient's spine to become further and further hyperextended The limit of extension varied with the patient's build, posture and hypertrophic changes in the spine When the patient complained of pain in the lumbosacral area, full hyperextension had been obtained After a few minutes, if hyperextension was carried a little beyond this point, the maximum was obtained Impending cord pressure during reduction was determined by motor weakness or shooting pain in the extremities Both were preceded by severe pain at the site of the fracture

For fractures of the lumbar spine a modification of the method of Davis was preferred The patient's trunk was covered with stockinette and placed in a prone position on taut canvas sling The ankles were padded with sheet wadding and slings applied The legs were gradually raised by a block and tackle attached to the ankle slings (Fig. 14) The patient retained his balance on the canvas sling by holding the suspending frame or table When maximum hyperextension had been obtained, a strip of felt was placed over the spinous processes, another about the upper chest and a third about the anterior pelvis A plaster jacket was then applied from the sacrum to the scapulae and from the anterior superior iliac spines to the sternoclavicular joints (Fig 15) A large window was cut out over the abdomen for the patient's comfort

In fractures of the dorsal vertebrae, the Dunlop sling method was used The

patient was placed on the hammock frame with the occiput on one table, the low back and hips on a second beneath the hammock, and the legs on a third. A canvas sling 6 inches (1524 cm.) wide was passed beneath the dorsal spine at the site of the fracture and attached to

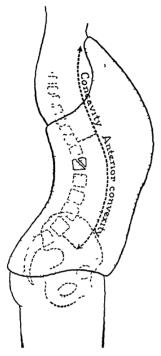


Fig 15 — Diagram showing extent of plaster jacket used in the treatment of lower dorsal and lumbar vertebral fractures (Courtesy, American Journal of Surgery, December, 1937)

a spreader suspended from the overhead pulley block. The arms were held by assistants *Hyperextension of the dorsal spine* was obtained by the lift directed by the sling beneath it (Fig. 16). The table beneath the hips was removed and a jacket was applied from pelvis to include the chin and occiput (Fig. 17).

In the absence of paralysis and if the fracture lay in the anterior portion of the vertebral body, the patient could be gotten up as soon as possible, in order to maintain muscle tone. Active spinal extension and abdominal retraction ex-

ercises were started within a few days and kept up throughout treatment. The jacket was worn four months. In severe crush fractures the jacket was worn an extra month. If the patient lost weight and the jacket became loosened, another was applied in the same manner as before. After the plaster jacket, a high back brace was worn for a month and the exercises pushed. Additional exercises to correct the pelvic rotation were then given.

Dislocations of the vertebrae had to be accomplished with the greatest care to avoid cord or nerve root damage *Reduction* was attempted by the hyperextension method. At the first sign of cord or nerve root pressure, the patient was slowly returned to the former posi-

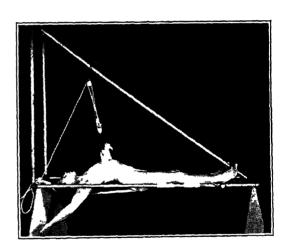


Fig 16—The hammock frame adapted to the sling method of obtaining dorsal hyperextension Reduction is very much more difficult in the upper ten dorsal vertebrae and greater forces are necessary. The same mechanism may be employed with tables, as described in the text (Courtesy, Amer Jour of Surg., Dec., 1937.)

tion and a jacket applied for immobilization. Failure of extension to reduce a dislocation was due to locking of the articular processes. These processes could be freed by open operation, under a local anesthesia, with the patient lying in anterior half of cast. This should not be

attempted by an inexperienced surgeon As soon as the facets were freed and the spine hyperextended, a jacket was applied and the treatment was the same as in the fracture

Fracture of the transverse processes was not a grave injury. At times a few days' rest in bed was indicated, then firm

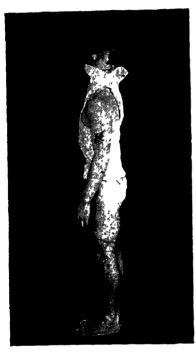


Fig 17—Jacket employed in fracture involving the upper ten dorsal vertebrae Because of the anterior concavity of the spine in this region, it is necessary to support the entire superincumbent weight by the jacket To this end, the neck, chin and occiput must be included (Courtesy, Amer Jour of Surg, Dec , 1937)

adhesive strapping renewed every five days for several weeks. Extensive haematoma necessitated a plaster jacket. Exercises were started in three weeks. Maximum disability for transverse process fractures was eight weeks.

Fractures of the Pelvis

L M Rankin⁵³ reviewed a series of 449 fractures of the pelvis from 1907 to 1934, with ages varying from 1 to 80 years. Of this series 144 patients were

discharged as well, 249 as improved and only four as unimproved. Forty-one died and 11 released themselves. Fractures of the pelvis were usually multiple but the ilium and the superior ramus of the pubis were fractured most frequently. The treatment of choice for these 449 cases was *suspension* in a hammock with *traction* on the lower extremities. There was leg shortening in 25 per cent, which could have been avoided by proper traction.

Os Acromiale

Frank Liberson⁵⁴ presented 21 typical cases of os acromiale which occurred in 1800 roentgenographic examinations of shoulders This condition he found to be present in 27 per cent of the shoulders examined A differential diagnosis could be made on the basis of 62 per cent of os acronuale occurring bilaterally The edges of the cleavage line appeared uniform and smooth in the x-ray as contrasted with the sharp ragged edges in the case of fracture The position of the shadow was at the same or higher level than the body of the acromion, whereas in the fracture this fragment was apt to be at a lower level Fractures of the acromion were relatively infrequent and practically always associated with another mjurv

Fracture of the Head of the Humerus

Treatment and Results — J W Sever⁵⁵ reported 91 cases of fractures of the head of the humerus treated by various methods. He concluded in fractures of the external tuberosity without displacement, no reduction was necessary. When there was separation of the external tuberosity, outward rotation, abduction and elevation would replace the fracture surfaces. When there was dislocation of the head with a fracture separa-

tion of the greater tuberosity, reduction of the dislocation was required. Dr. MacAusland's method of abduction, outward rotation and elevation with early motion gave the best results In comminuted fractures of the head and transverse fractures of the head with displacement of the fragments, the author advocated traction under general anesthesia, and manipulation under the fluoroscope using the stockinged foot in the axilla as a counter force and as a fulcrum to reduce the inward displacement of the distal fragment Traction in line with the body and also in outward rotation and abduction was necessary to reduce the fragments

If the fracture was impacted, it was best left alone provided the position was quite satisfactory Dr. MacAusland stated that "ten days to two weeks is a sufficiently long time to insure enough union so that the patient may be allowed up and about in an ambulatory splint that maintains the reduction"

Fracture Dislocation Upper End of Humerus

G W Leadbetter⁵⁶ reported 17 cases of fracture dislocation of the upper end of the humerus Such fracture dislocations occurred after severe trauma, such as automobile accidents or falls from Two cases were treated satisheights factorily by suspension traction and gentle manipulation from day to day Ten cases were reduced with fluoroscopic control by means of strong traction and digital manipulation Five cases were treated by open reduction, in one of these the head was completely removed and a weak, unsatisfactory shoulder resulted Plaster fixation was used after reduction Cases reduced by manipulation had better results and shorter hospitalization Open reduction was difficult and caused considerable trauma and resulted in permanent damage to the joint Early reduction was important. A delay of a week increased the difficulty of reduction.

Simplicity in Treatment of Fractures of Upper End of Humerus-E. L Eliason and J. Johnson⁵⁷ reviewed 100 cases of fractures of the upper end of the humerus. Perfect reduction was not necessary to procure the desired function In 89 of the 100 cases some type of fixation or operation was used Simple fixation at the side was used in 63 or 70 per cent of these cases The arm was maintained in abduction in 19 cases or 21 per cent Operation was performed in five cases Traction in bed was used in two cases. Of the 100 cases there was a follow-up of 56 patients and it was found that 894 per cent of these cases had a satisfactory result. In elderly and debilitated individuals with fractures of the upper end of the humerus, simple fixation at the side was the most valuable

Fractures of Shaft of Humerus

A D LaFerte and M G Rosenbaum⁵⁸ reported the clinical results of 58 cases of fracture of the shaft of the humerus treated by hanging cast method This was originally described by J A Caldwell 58a Not all fractures of the humerus were considered suitable for treatment Badly comminuted fractures of the head and fractures involving the condyles or supracondylar area were omitted from this series The method consisted of early manipulation under deep anesthesia on a fluoroscopic table, if there was displacement of the fragments Strong force was applied to the arm in two directions First, by traction with a flannel band passing around the flexed elbow of the patient and around the operator's waist, and, second, by pressure exerted at the fracture site at right angles to the shaft, to correct the

medial or lateral displacement. Countertraction was obtained by a sheet around the thorax. The "hanging cast" was applied when a good reduction was evident under the fluoroscope. This was done by holding the arm in the abducted position with the elbow flexed and three rolls of plaster six yards long and six inches in width were used. The bandage extended from the wrist to the axilla A plaster loop was incorporated at the distal end to permit suspension from the neck. Roentgenograms were taken the next day and at two week intervals.

Fractures were classified according to those in the upper third of the humerus and the middle and lower thirds Twentythree fractures of the upper third of the humerus with good or fair position in individuals from 5 to 86 years were treated In nine cases the patient was not hospitalized Slipping of the fragments occurred in only three cases The treatment of ten fractures in the upper third of the humerus with various displacements were treated by this method Two cases failed, three had an open operation followed by a "hanging cast" and five were satisfactory In 33 fractures of the surgical neck of the humerus good results, both anatomical and functional, were obtained Sixteen fractures involving middle or lower third of the shaft offered considerable concern and careful watching because of circulatory disturbance brought on by the acute flexion of the elbow However, all were satisfactory, except one badly comminuted fracture Union occurred in all cases One had a radial palsy Twelve cases had various degrees of angulation Following removal of the cast, physiotherapy was used in 20 out of 58 cases This was found to be necessary in fractures which occurred at or near the surgical neck

This method undoubtedly is best used in fracture cases which have little dis-

placement It certainly is not applicable to spiral fractures or badly comminuted fractures. A great deal of caution is necessary in handling fractures about the distal third of the humerus by this method, due to the danger of circulatory complications

Ununited Fractures of Shaft of Humerus

W C Campbell⁵⁹ reported the endresults in 50 cases of ununited fractures of the shaft of the humerus One patient with an oblique fracture line was treated by transfixation of the fragments with autogenous bone pegs union resulted The remaining 49 were treated by the application of a massive inlay graft from the tibia secured by autogenous bone pegs In addition to this, a strip of endosteum was placed within the medulla and bony shavings were placed about the site of the fracture There were three failures in the 49 so treated There were no nonunions in the four patients in whom postoperative infection occurred

Colles' Fracture

R MacAusland⁶⁰ attributed the unsatisfactory results from Colles' fracture to failure to restore the anterior palmar tilt of the lower end of the radius A Colles' fracture was a simple one to reduce and as Dr MacAusland stated there was little excuse for a poor result In reducing a fracture of this type, the deformity was first increased by pulling the wrist back and forcing the lower end of the radius toward the ulnar side to overcome the radial displacement Then the radial fragments were pushed forward into position, forcing the wrist to fall into flexion. If the deformity was only partially reduced, the wrist joint remained weak and chronic hypertrophic changes with loss of function developed

Fracture of the Carpal Scaphoid

Joseph H Burnett⁶¹ reviewed 100 patients with fracture of the carpal scaphoid treated at the Boston City Hospital Emphasis was placed upon the importance of protection of severely sprained wrists by means of splint or leather wrist strap until roentgenograms

included the palm of the hand, the proximal digit of the thumb and a few inches above the wrist. This left the fingers free. The immobilization was maintained for six to eight weeks. In cases where there was marked separation of fragments and in those which the wrist was crippled by months of use with non-

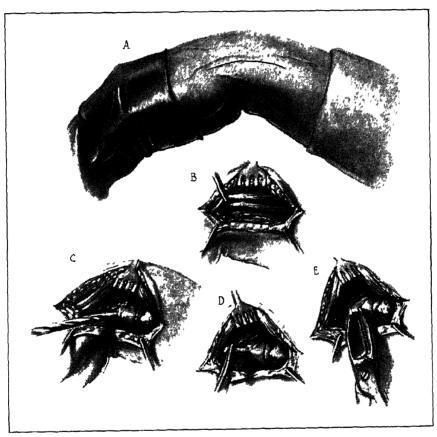


Fig 18—Operative technic (Courtes) Journal of Bone and Joint Surgery, October, 1937)

proved that a fracture of the scaphoid did not exist. This was necessary as many scaphoid fractures were merely cracked across at the start and after some weeks a heavy line of absorption appeared by roentgenogram. As soon as the diagnosis had been established in the fresh cases, the hand was immobilized in a plaster bandage in the cock-up position with slight radial flexion and with the thumb in abduction. The bandage

union, open operation and bone pegging was advised

The technic was as follows Through a lateral incision midway between the palmar and dorsal aspects of the radius, the wrist joint was exposed. After the joint was exposed, the wrist was placed in acute palmar flexion and ulnar deviation, which placed the scaphoid in the middle of the wound. The fracture line was identified and a drill hole one-

Johansson Tabulation According to Anschultz's Scheme of Classification

| Under 60 Over 60 Totals | Total Cases 53 112 (66) 165 | Deaths 1 18 (15) 19 | Cases Operated 52 94 (51) 146 | Nonunion 0 8 (5) 8 | Arthritis 1 1 (1) 2 | Aseptic Necrosis 1 1 2 |
|--|--------------------------------------|---------------------|---|-----------------------------|-------------------------|------------------------------------|
| Intertrochanterics Under 60 Over 60 Totals | | | Total Cases Deaths 3 0 11 (7) 0 14 0 | | Nonunion 0 0 0 | |

Figures in parenthesis denote cases over 70 years of age

fourth inch (635 mm) in diameter was made through the distal into the proximal fragment. A peg of bone was obtained from the tibia and tapped into the drill hole and the end was smoothed down to the surface of the scaphoid with rongeurs. The results of this procedure were reported excellent. Strong wrists, free from disability other than limitation of dorsi flexion, were obtained (Fig. 18)

Fractures of the Neck of the Femur

Willis C Campbell⁶² stated that the treatment of nonunion of fractures of the neck of the femur depended upon the age and general condition of the patient, and upon the viability of the head The tibial bone graft was considered as the ideal procedure in these cases He reported a series of 36 cases with solid union in 20 patients. One death occurred in this series There were eight failures. In another series of 35 cases, in which the Whitman, Albee or Brackett reconstruction operation was performed there were eight failures, 14 excellent results, one death and no follow-up on 12 because of the short time since operation

In another article on fractures of the neck of the femur in general, Willis C Campbell reported the use of the Smith-Petersen nail in 35 cases—11 open and 24 blind nailings. Only 19 cases were

followed through, but of these there was 100 per cent solid bony union

Lawson Thornton of Atlanta reported 100 per cent solid union in a series of 30 cases of fractures of the neck of the femur in which the Smith-Petersen nail was used Brewster's series reported 89 per cent excellent results

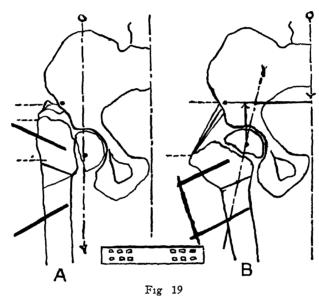
J Albert Key⁶³ described the insertion of a Smith-Petersen nail for intracapsular fractures of the neck of the femur The fracture was reduced by the Leadbetter method X-rays were taken for check-up, local anesthesia was given A six-inch (1524 cm) incision was made over the lateral surface of the femur and a drill inserted Another set of roentgenograms were then taken to check the depth and angle of the drill If satisfactory, the drill was removed and the pin inserted in the drill hole so that it penetrated the head from the neck a little below the midline The distal fragment was firmly impacted and another check-up film was taken Postoperative fixation was used Weight-bearing began four weeks after the operation but crutches were used for at least three months

Operative Treatment and Result in Fractures of the Neck of the Femur—Sven Johansson⁶⁴ reviewed 179 cases of which 165 were intracapsular fractures of the femoral neck and 14 intertrochanteric One hundred and

twelve of the former were over 60 years of age and 53 under 60 In this group there were 19 deaths. One hundred and forty-six cases were operated upon and there were but eight cases of nonumion

The method consisted first of checking the reduction by means of anteroposterior and lateral x-ray films and then obtaining a central position in the femoral neck and head of the Kirchner

cedure was particularly adaptable to those cases of delayed union or non-union with coxa-vara deformity which had instability and varying degrees of pain. The principle was to produce a valgus angulation in the trochanteric region which would place a direct thrust of weight-bearing, transmitted through the femur, upon the fracture line The 13 cases of this study were divided into



A The oblique insertion of screws (Riedel) allows greater working space than when the screws are introduced perpendicularly to the shaft, as in a true Schanz osteotomy. Note relaxation of muscles attaching to greater trochanter due to upward riding. Inefficiency of these muscles is also due to loss of lever action.

B Shows screws parallel after angulation of femur and securely fixed by use of Riedel plate. Note effect on musculature following osteotomy. (Courtesy, Journal of Bone and Joint Surgery, October, 1937.)

guide wire before driving in the Johansson modification of the Smith-Petersen nail. If check-up x-rays failed to show a satisfactory position of the fracture or a change in the position of the nail, reoperation was done. Nineteen cases in this series had a second operation.

Herman C Schumm⁶⁵ described his technic for a **Schanz osteotomy** in fractures of the neck of the femur The indication for this procedure was disability due to instability of the hip The pro-

two groups, first, cases which had developing coxa-vara deformity at the fracture site which indicated a prospective nonunion, and second, cases of definite nonunion with absorption of the neck in which there was upward riding of the shaft. In the first group the osteotomy was placed just above the lesser trochanter, whereas in the second group it was placed a few centimeters below the lesser trochanter. An anteroposterior roentgenogram taken with the affected

leg in abduction was of importance in determining the degree of angulation to be obtained in the osteotomy. The operative technic consisted of a longitudinal incision over the trochanter. The special Schanz screws were placed in oblique positions, one above and one below the proposed site of osteotomy. After the

At the end of the eighth week the case was removed and a check-up roentgenogram was taken. If the callus appeared insufficient a light plaster spica was reapplied holding the hip in abduction. The first or second week following the removal of the cast the leg was exercised by means of sling pulleys and baths



Fig 20—Ununited fracture of the femur four months following fracture (Courtesy, Journal of Bone and Joint Surgery, October, 1937)

wedge of bone was resected from the osteotomy site and correction was obtained by bringing the bone edges together, the screws were parallel. The wound was closed and a Riedel plate was placed over the screw ends to aid in maintaining the position. A large plaster spica was applied including the affected leg to the toe and the well leg down to the knee (Figs. 19, 20 and 21).

in a Hubbard tub. The patient was permitted weight-bearing with crutches in the tenth or twelfth week.

Difficult Ankle Fractures

Bryan McFarland⁶⁶ divided the difficult ankle fractures into recent and late Of the recent fractures, the bimalleolar and the anterior margin of the tibia were the most difficult. The bimalleolar fracture was of both malleoli at the same level as the upper astragalar surface. This was difficult to reduce as it was so mobile that there could be overreduction in any direction. The author felt that the best way to reduce such a fracture was to feel the edges of the internal malleolar fracture with the thumb by pressing

posterior marginal a large fragment joined the shaft with the astragalus articulating with it in this displaced position, leaving an anterior buttress. The treatment was to remove this buttress so that a fair range of movement could be regained. The posterolateral dislocation fracture, up to six months, was im-

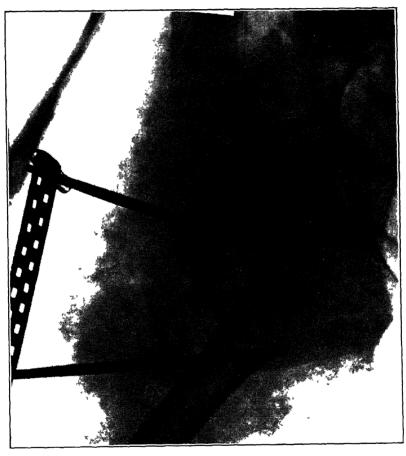


Fig 21—Same patient as in Fig 20, showing position of fracture following a low Schanz osteotomy, with Schanz screws and Riedel plate in place (Courtesy, Journal of Bone and Joint Surgery, October, 1937)

deep into the swelling and then gently reducing the fracture

The anterior margin fracture was displaced by upward and plantar flexion which caused the astragalus to ride forward

In the late type, in which there was malunion, were the posterior marginal and the posterolateral fractures. In the proved by reconstruction of the joint, but after six months elapsed, arthrodesis of the ankle joint was the only procedure that could give satisfaction

Fractures of the Patella

In fractures of the patella R Brooke⁶⁷ recommended *complete removal* of the patella This operation had been done on

30 patients. In the cases followed, the injured leg was stronger than the uninjured in resisting flexion. This was a radical procedure for fractures of the

was closed by interrupted sutures. The knee was immobilized in extension for two or three weeks. Normal function was regained in six weeks.



Fig 22—Patient turned on side opposite injury. The sandbag is placed under the inner side of the injured heel. A sterile rolled towel is placed beneath the external malleolus. Then, with solid heavy blows, impaction is broken up and the piled-up bone beneath the external malleolus is pounded down. (Courtesy, Journal of Bone and Joint Surgery, July, 1937.)

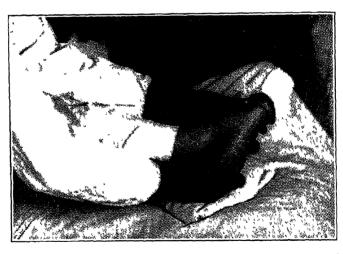


Fig 23—This illustrates how easily the thumb can be pressed into the depression beneath the external malleolus and the heel can be molded by the fingers after the pounding (Courtesy, Journal of Bone and Joint Surgery, July, 1937)

patella but the end results had been so excellent the condition warranted this surgical method A vertical incision was made, through which the bone fragments were removed. The gap in the tendon

Brooke made a very interesting study on the cadaver From the standpoint of comparative anatomy, the patella was a vestigial structure and that function did not influence its development or growth The bone formed behind the quadriceps tendon and became attached to it secondarily, but it did not develop within the tendon. This work on the cadaver by means of drums and pulleys showed

illustrated by photographs of patients following the operation of complete removal of the patella, which the author stated should be done 48 hours after the injury has occurred

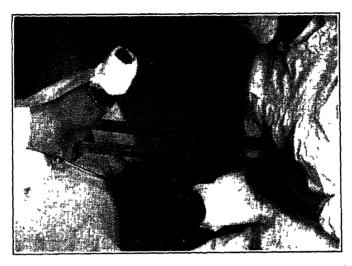


Fig 24—With a scalpel, small incisions are made about an inch or so above the apex of the heel. The tongs are driven in and locked, and traction is then made in a rotary fashion, beginning downward and swinging upward, with countertraction exerted just proximal to the cuboid joint (Courtesy, Journal of Bone and Joint Surgery, July, 1937)

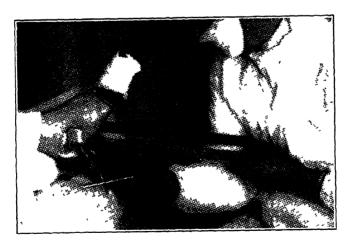


Fig 25—The os calcis is remolded systematically from the external malleolus downward by means of the Forrester clamp. Again traction is exerted downward and upward with counterpressure in the os calcis and cuboid areas. (Courtesy, Journal of Bone and Joint Surgery, July, 1937.)

that extension of the lower leg through a right angle took place more rapidly without the patella and that there was less resistance to a weight applied against the moving force. The article was well

Fracture of the Os Calcis

Conservative Therapy — Otto J Hermann⁶⁸ reported the follow-up results of 152 acute fractures of the os calcis treated at the Boston City Hospi-

of both the fractured and the uniquired os calcis for comparison, as well as a lateral and anteroposterior x-ray film of the lumbar spine, as fractures of the lower thoracic or lumbar vertebrae were found to exist in ten per cent of the cases From the roentgenograms of the os calcis it was possible to determine the extent of the lateral expansion and



Fig 26 — A low plaster-of-Paris cast 18 finally applied with the foot somewhat inverted and in plantar flexion. While this cast is hardening, pressure is brought to bear over the pads. (Courtesy, Journal of Bone and Joint Surgery, July, 1937.)

the amount of communation The foot and lower leg were encased in a "pillow" splint and elevated for one to ten days until the local reaction had subsided Reduction was done under a general anesthesia. The patient was placed on the side opposite the injury with a sandbag under the inner side of the heel. A tightly rolled towel was placed beneath the external malleolus. With a wooden mallet solid heavy blows were applied to the lateral aspect of the os calcis in order to obtain disimpaction. (Fig. 22). The os calcis was then molded by hand

and the various motions tested (Fig 23) If satisfactory, small stab wounds were made in the upper posterior portion of the heel where there was no fracture line and tongs were driven in and locked Traction was then applied in a posteriorlateral direction, swinging distally to the plantar surface of the foot (Fig 24) The tongs were then removed and a Forrester bone clamp was used to compress the os calcis (Fig 25) Checkup x-rays were then advised to determine satisfactory position before applying a plaster cast Small dressings were applied over the stab wounds and a roll of felt 4 by $1\frac{1}{4}$ inches (10 by 3 cm) was placed at a slightly oblique angle beneath each malleoli A plaster-of-Paris bandage was applied with the foot in slight inversion and extreme plantar flexion (Fig 26) Every two weeks the cast was removed and new pads applied beneath the malleoli, up to the tenth or twelfth Then a "special ambulatory os calcis splint" was applied. Then daily massage, active foot and ankle motions, gradually increasing toe and heel and foot rocking exercises, supination plank-walking, and radiant heat or hot soaks were begun. Two weeks later full weight-bearing without crutches or with "ambulatory splint" was started A one-sixth inch (323 mm) Thomas heel and well-fitted anterior and plantar arch pads were added to the shoe At the end of the twentieth week the "ambulatory splint" was discarded and strennous foot exercises and increased walking on rough surfaces permitted Seventythree per cent of the cases had good results, 14 per cent fair and 13 per cent poor The poor group included those who during the first three or four weeks of weight-bearing had persistent pain in the subastragalar, calcaneo-cuboid or astragaloscaphoid joints These generally required a subastragalar arthrodesis. In only one case was it necessary to lengthen the tendo achillis.

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THORACIC SURGERY

By GILSON COLBY ENGEL, M D.

BRONCHIECTASIS

Although the incidence of small occasional hemoptyses, especially during exacerbations of bronchiectasis, is generally admitted, less emphasis has been placed on the frequency of extensive, life-threatening hemorrhage, which may end fatally D S King1 describes several cases illustrating the significance of hemorrhage in this condition. In one case treatment for wrongly diagnosed pulmonary tuberculosis was pursued for more than four years Except for the failure to demonstrate the tubercle bacilli in the sputum, the symptoms closely resembled those of pulmonary tuberculosis The patient had suffered from hemoptysis for years and had experienced several severe hemorrhages Unfortunately the rest cure prescribed for the suspected tuberculous disease was without effect on the bronchiectasis Finally a lower left lobe bronchiectasis was diagnosed and after an ineffective temporary phrenic paralysis, a left lower lobectomy was performed with splendid results Hemorrhage may be not only the first, but also the only symptom of bronchiectasis, which may precede or coincide with tuberculosis thus adding to the diagnostic confusion A marked compensatory emphysema of the upper lobe in atelectasis of the lower lobe, especially a unilateral emphysema, should rouse suspicion of involvement of the lower lobe

Among the less usual localizations of bronchiectasis, King mentions the "pancaked" middle lobe, right middle and left lower lobe bronchiectasis, spread from the lower to the upper lobe and extensive involvement of all five lobes lobectomy is postponed in suitable cases, there is risk of severe hemorrhage or pneumonic infection Cases in which death was due to metastatic brain abscess, pulmonary edema and cor pulmonale have been reported. Whereas very little satisfaction was obtained from medical treatment of bronchiectasis, E D Churchill² has been largely responsible for the striking success obtained with lobectomy in this clinic He does not advocate preliminary phrenicectomy and believes that except in case of hemorrhage, there is no real indication for artificial pneumothorax He is convinced of the value of postural drainage, general hygienic measures and proper attention to sinus infection as well as other infections Churchill prefers to operate on these cases during the period between the first of May and the middle of December, owing to the increased incidence of infections during the winter and early spring months Diagnostic bronchoscopy should always precede lobectomy, and special attention is also given to postural drainage immediately before operation Where bronchiectasis is well established operations on the sinuses cannot be expected to give much satisfaction, but where areas of chronic pneumonitis are associated with chronic sinusitis, a removal of the focus of infection may have a prophylactic value. Operation for obstruction of the sinuses before lobectomy is advisable, but as a rule lobectomy should precede any radical intervention on the nasal passages Churchill describes in detail the technic of one-stage, two-stage and middle-lobe lobectomy He recommends a delayed second stage in the two-stage procedure, postponing the actual removal of the lobe for at least six weeks after the first stage operation The one-stage operation is indicated in children, in bronchial stenosis, in middle lobe resections, in severe hemoptyses, for cutting into infected lung tissue when freeing adhesions, for obliterated pleural space or strong adhesions binding the upper lobe to the chest wall, for lobar atelectasis in absence of upper lobe emphysema, and for draining thoracotomy sinus of bronchocutaneous fistula

The two-stage operation is indicated in adults with free pleural space, in febrile patients with active pneumonitis, in patients treated for a prolonged period with artificial pneumothorax without adherent upper lobe and in patients with bilateral disease with free pleural space

Fine silk ligatures and sutures are used instead of chromic catgut within the pleura. A case of bilateral lobectomy is reported and attention drawn to the fact that the coincidence of bronchiectasis and situs inversus is more common than suspected. Also a case of one-stage total pneumectomy is described in a case of bronchiectasis of both lobes of the left lung. The stump of the lung was handled as in lobectomy by chromic catgut sutures, and the pleural cavity was drained with a catheter. After a long convalescence from empyema and bronchial fistula, for which thoracoplasty

was performed, an excellent recovery was reported There has been no mortality in the last 30 cases treated by this method of one-stage or two-stage lobectomy in the clinic.

Likewise J. V Bohrer³ agrees that lobectomy is the method of choice for treatment of bronchiectasis. He uses inhalation anesthesia and the general utility incision of Lilienthal. Hemostasis is effected by ligation of the vessels or electrocoagulation The diseased tissue is removed by clamping and dividing at the stump, after which the stump is repleuralized The adhesions in the interlobar fissures are divided to separate the upper and lower lobes Also the adhesions to the diaphragm and in the posterior gutter are divided, as well as the pulmonary ligament The lobe is then amoutated and the wound carefully packed with gauze saturated with acriflavine The pedicle vessels are ligated individually with mattress sutures and the tourniquet removed The stump is then closed Leakage from the stump may be exposed by increasing the intrapleural air pressure The oozing serous fluid is aspirated and a drainage tube inserted through a stab wound in the ninth intercostal space in the posterior axillary line The oxygen tent is then applied for 24 to 48 hours. To close the wound, the ribs are approximated with two 20-gauge silver wire pericostal sutures, and the muscles are closed in layers with interrupted sutures. If there is much soiling the skin is not sutured

R H Overholt⁴ draws attention to the fact that as bronchiectasis is more often bilateral than unilateral, affecting the two lower or the left lower and right middle lobes, bilateral lobectomy will have to be considered as an intervention in the future more frequently than pneumectomy. He describes a case in which a successful trilobectomy was

performed in a patient who had been an invalid for 16 of her 19 years of life The three bronchiectatic and atelectatic lobes were functionless and a source of potential danger On June 1, he did the first stage of a right lower and middle lobectomy On September 27 the first stage of a left lower lobectomy was done and on November 13, the second stage of the right lower and middle lobectomy Finally on March 3, 1937, the second stage of the left lower lobectomy was completed Thanks to this operation, the patient was enabled to take part in ordinary social activities, the danger of progression of the disease was diminished, the lung volume and vital capacity were improved and the function of the remaining lobes improved

According to Brunner, as good results are not to be expected from artificial pneumothorax in bronchiectasis as in tuberculosis because the rigid bronchicannot collapse so easily. Some cures have been effected but the pneumothorax has to be continued for a much longer time than in tuberculosis (12 vears or more) with the continuous danger of exudate and infection. Once the expectoration has ceased and the patient has recovered his strength, an extrapleural thoracoplasty should be done

M P Susman⁵ is of the opinion that simple, non-operative measures may suffice in cases in which the bronchiectasis is not progressive, especially if the infection of the nasal sinuses is properly treated. He reports a series of 28 lobectomies and four thoracoplastics. The general indication for lobectomy is progressive bronchiectasis confined to one lobe or to the lower and middle lobes of the right side. Total pneumectomy is indicated in moderately advanced bronchiectasis of the whole or greater part of one lung, if not hopelessly adherent

to the chest wall. Thoracoplasty is preferable in early uncomplicated cases of unilateral type Cautery excision is best for complicated advanced unilateral cases. The anesthesia may be spinal or cyclopropane preceded by hypnotics. Up to 1935, 107 lobectomies for bronchiectasis were performed at the Brompton Hospital, with 15 deaths. Three patients in whom total pneumectomy was performed, recovered.

There is still some question as to whether it is best to use a one- or twostage operation in cases of single lobe involvement (S W Harrington⁶) The two-stage operation is often followed by empyema and bronchial fistula and convalescence is greatly prolonged as compared with the one-stage procedure, in which the bronchial stump will usually heal by primary intention without residual disability Harrington describes such a case treated by the one-stage operation in detail, in which, in spite of marked infection of the lower lobe, the healing was prompt and the upper lobe quickly expanded with a hospitalization of only 18 days after operation

E I O'Brien⁷ reports a series of 15 cases of bronchiectasis in which the onestage lobectomy was performed In his experience the most serious sequelae of one-stage lobectomy have been hemorrhage from the stump and empyema due to bronchial fistula For this reason he has given special attention to ligature of the stump and facilitating a more rapid expansion of the remaining lobe Less postoperative pain is experienced if, on opening the thorax, a segment of rib is removed instead of merely cutting the ribs A modification of the Brunn-Shenstone technic is used. If the lobes are free, the proximal snare is applied around the hilus before manipulating the lobe Otherwise adhesions must be freed, and the lobe grasped with the lung forceps while the snares are placed The distal snare must be so placed as to leave sufficient space for safe suturing. After closing the stump, and simultaneous with the removal of the proximal snare, four strands of catgut are tied in the groove where the stump has been crushed, while the snare was in place. Three mushroom catheters are placed in the pleural cavity through stab wounds and the chest tightly closed, one catheter in the axilla, one above the diaphragm anteriorly and one posteriorly at the stump Suction is applied to the catheters upon the patient's return to the room by means of a mercury reduction chamber placed in the circuit between the closed sterile dramage bottle and the water pump on the faucet Negative pressure is continued for three weeks, when all tubes except the one at the stump are removed. The remaining tube is made into an open drain In four of the 15 cases the disease was bilateral, and when unilateral, confined to one lobe in seven and to more than one lobe in four There was one death from pulmonary embolism which could not be attributed to the onestage operation No permanent fistulas remained In eight patients there was no evidence of bronchial opening In seven patients the bronchial stump opened at an average of 119 days after operation and the fistulas closed in from a few days to several months A small empyema developed about the stump in all cases. In three wider drainage was required The lung was fully expanded in 24 hours in all patients except one It was necessary to aspirate in only four cases There was no hemorrhage from the stump Subcutaneous emphysema developed in two cases. In cases of bilateral involvement, the frequent use of the bronchoscope and intratracheal catheter will greatly diminish postoperative hazards In some cases of

bilateral involvement, removal of the worst side will result in such improvement that further operation is not desired Bilateral lobectomy with both lower lobes functioning might prove difficult, whereas if they have been collapsed for some time no serious change would ensue.

LUNG ABSCESS

Owing to the high mortality attendant upon surgical treatment of lung abscess in former years internists have become prejudiced against early surgical drainage as a method of treatment for lung abscess It is said that 20 to 50 per cent of cases will recover without surgical drainage If, however, an abscess fails to drain or is drained only inadequately through a bronchus, the manifestations of infection will persist and recovery will not take place The time to allot to expectant treatment is difficult to judge Operation done early in the acute septic stage has a high mortality and should be avoided If an abscess is going to heal spontaneously it usually shows a tendency in this direction during the first six to eight weeks after onset. If such a tendency is not manifest external drainage should be established. In the series reported by R L Moore's 109 operations were done for 37 abscesses in 34 patients Twenty-nine of the 34 primary abscesses had existed for more than six weeks before the first operation, 29 for more than two months, 22 for more than three months. 13 for more than six months, seven for more than one year, three for more than two years and one for 15 years Fifteen were in the upper lobe, four in the right middle lobe, 11 in the right lower lobe and four in the left The large percentage of lower lobe upper lobe abscesses is interesting because of the belief that drainage through

a bronchus is more likely to effect a cure in abscess of the upper lobe Sixtyeight per cent of the cases surviving operation failed to heal satisfactorily after simple drainage and had to be subjected to complicated and hazardous procedures If operation is done sufficiently early simple drainage will suffice For this reason the co-operation of the internist and surgeon is urged from the beginning The abscess may be localized by means of the roentgen rays If the patient is placed in a slight Trendelenburg position at operation, aspiration of exudate into the lungs may be prevented In most cases it will be found best to perform the operation in stages

First generous segments of two or more ribs are resected including the periosteum, intercostal muscles and thoracic fascia so as to expose a wide area of parietal pleura. The wound is then dressed with silk and iodofoim gauze tampon to stimulate the formation of adhesions. If the abscess has not been satisfactorily located, safety pins may be fastened to the pleura as markers for subsequent roentgenograms. Six to eight days later the cavity is located by aspiration and opened with the needle in situ

Electric cautery unroofing of the cavity is followed by cutting away of the tissue until the cavity is reached. Suction is then applied through a small opening and the contents evacuated at once to prevent aspiration into uninvolved portions of the lung. After drainage has been established the wound should be dressed at frequent intervals.

The position of the deeper pockets may be ascertained by roentgenography, after injection of lipiodol through the trachea or wound. The operator then carefully cauterizes in one or two stages along the sinuses. Intervening tissue is first coagulated and then excised piecemeal

until all pockets have been opened. If the cavities are in the periphery of the lobe there may be slight bleeding, but in the central cavities, which are larger, there is real danger of hemorrhage. In this area cauterization is contraindicated. The danger of air embolism is also greater from the central area.

Once drainage is obtained the wound is given ample time to heal If treatment has not been delayed too long healing will be prompt, otherwise residual cavities with fistulas will form. When efficient dramage is not obtainable by the cautery, lobectomy remains the only curative procedure The choice between closure of the wound and lobectomy depends on whether there is a sufficient amount of lung tissue left to make closure possible If the cavity extends into the region of the hilus, closure is usually unsuccessful and lobectomy is preferable The author uses Lebsche's procedure for closing the wound with residual cavity and fistula

In the latter, lobectomy is indicated when there is extensive fibrosis of the lung making closure impossible. In two of four cases it was possible to amputate the lobe without opening the free pleura. In the other two, although the free pleura was opened and some collapse occurred, the remaining dead space was satisfactorily obliterated. Fifteen of the 21 operations of lobectomy were for bronchiectasis, one for tumor which proved to be an encapsulated abscess, one bilobar lobectomy for carcinoma and the other four for chronic abscess of the lung. All are alive and well

The adhesions were found more extensive than usual in bronchiectasis, but were separated without great difficulty and considered as an asset on account of their stabilizing effect upon the mediastinum. After lobectomy in bronchiectasis, there are often stormy symptoms

and obstruction of the bronchi, but these It is always do not occur in abscess best to establish efficient drainage before considering lobectomy Local anesthesia is preferable because it abolishes pain without abolishing the cough reflex. For resection of the ribs in the first stage, paravertebral nerve block with local novocam infiltration is recommended. For cauterization in the second and subsequent stages, an anesthetic may occasionally be needed. If the patient is apprehensive a general nitrous oxide anesthesia combined with avertin is in-Avertin must be avoided in dicated cases with abundant sputum because of the danger of aspiration during the long period of unconsciousness after operation

The complications of lobectomy include hemorrhage, pneumonia, empyema, cellulitis of the chest wall and air embolism Pneumonia is the most frequent complication and is usually due to aspira-Severe hemortion during operation rhage is not uncommon and is more easily controlled in the peripheral parts of the lung It may occur when a vessel has been insecurely ligated in the chest wall, or after cauterization in the central lobes where the vessels are very Hemorrhage is also known to occur from eight to ten days after operation when the coagulated tissue separates Empyema should not develop if the abscess is not opened until after the lung is securely adherent to the chest wall If loosely adherent, the lung may be loosened during a coughing attack or Air embolism may be at operation avoided by thorough coagulation before cutting

Other complications include osteomyelitis of the ribs, steinum, infection of a costal cartilage and persistent sinuses due to residual cavities of the pleura at the site of operation caused by regeneration of bone bridging over the pleura and

forming a dead space, thus preventing the soft parts of the chest wall from being drawn in during healing. This is due to inadequate resection of the rib and periosteum at the first stage. In abscesses located posteriomedial in the paravertebral gutter it is important that rib segments be resected as far back as the transverse process of the vertebrae to prevent formation of a shelf. Infection of the cartilage may be prevented by resecting the entire cartilage at the first stage when upper or middle lobe abscess requires drainage anteriorly. Great care must be taken not to cut into the sternum as this involves risk of osteomye-Minor complications may require further surgical treatment that will delay recovery Of the 28 cases of 34 that survived simple drainage, spontaneous healing and relief of symptoms occurred in only nine The remaining 19 had to be subjected to cautery, pneumectomy or lobectomy Simple drainage was not enough to effect a cure in these cases because of extensive fibrosis and bronchiectasis due to the long period of medical treatment

P A Midelfart and J W Gale⁹ report 31 cases of pulmonary abscess About two-thirds of postoperative abscesses develop in the right lower lobe and only one-quarter of the nonpost-operative abscesses are located in this region. The latter are chiefly chronic, the average duration before operation being 41 months. Twenty-three were treated surgically and eight medically. The mortality in the operated cases was 52 per cent, in the nonoperated cases 50 per cent.

All the surviving surgically treated cases were either well or clinically cured on discharge, while only one case, and that a very acute one, was improved without open drainage. The operative mortality in 13 cases with single ab-

scess was 38 per cent, in the multiple abscess 70 per cent. The operative mortality in 14 cases of less than one year's duration was 28 per cent, while that in nine cases of more than one year's duration was 89 per cent. The longer the abscess has been present, the more likely it is to become multiple and both factors together and separately increase the operative and nonoperative mortality.

Chevalier Jackson¹⁰ repeats his plea for consultation among internist, surgeon, roentgenologist, pathologist and bronchoscopist in every case of suppurative disease of the lung At such a conference will be determined the diagnosis, the further diagnostic steps to be taken, the localization, the pathologic conditions present, the degree of natural drainage, the possibilities of improvement of peroral dramage by bronchoscopy, the advisability of instituting or postponing external drainage Jackson asserts that the bronchoscope has the same relation to intrathoracic disease that the vaginal speculum has to pelvic disease and may disclose conditions that can be treated medically, surgical conditions or suppuration that can be drained by the Although the bronchobronchoscope scope cannot enter the bronchioles, the bronchoscopist may by using the "tussive squeeze" remove pus and secretions from the periphery of all five lobes

Vertebrated aspirating tubes can be put up around the corner also into the upper lobe bronchi, but are necessary only in obstruction of the bronchi of the upper lobe. In such cases after the obstruction has been removed, and in all other cases the tussive squeeze will bring the pus down into the main bronchi from which it can easily be removed by aspiration. In abscess near the root of the lung bronchoscopic study and aspiration are indicated before resorting to external drainage of the root area. In

bronchial obstruction any procedure short of lobectomy distal to the obstruction is not to be advised until after the obstruction has been removed.

Bronchoscopy is indicated to remove bronchial obstruction in cases where obliteration of the pulmonary parenchyma distal to the obstruction is not desired As an aid in the treatment of lung abscess, it should be kept in mind that bronchoscopy not only drains the abscess but also the tracheobronchial tree The latter is not accomplished by thoracotomy In patients who have not been subjected to drainage of the tracheobronchial tree following thoracotomy, bronchoscopic aspiration and avoidance of all cough medicines are important in the after care of the patient Patients should always be given the chance of arresting the abscess in the acute or subacute stage by the aid of bronchos-The longer the abscess has existed the less is to be expected from bronchoscopic supervision of drainage

Catheter aspiration of lung abscess has often been successful and should be applied every few minutes or hours by the nurse in patients suffering from posttonsillectomy abscess. It is also of great value in patients with tracheotomy cannula In some cases tracheotomy might be considered with a view toward permitting more frequent aspiration Jackson concludes by emphasizing the fact that tracheobronchial aspiration of a lung abscess does not necessitate insertion of the tube into the abscess cavity. The procedure merely clears away the obstruction and affords a means of aspirating the pus as it is brought down into the main bronchi by the tussive squeeze

CARCINOMA OF THE LUNG

Reports of the increasing incidence of carcinoma of the lung are multiplying,

but most writers agree that this increase is apparent rather than real and probably owing to advances in diagnosis. Early diagnosis remains here, as in carcinoma elsewhere, the goal toward which all efforts must be directed if mortality rates are to be reduced Chevalier L Jackson and F. W Konzelmann¹¹ emphasize the value of bronchoscopic findings in bronchial carcinoma whether positive or negative In cases with negative biopsy, the appearance of surrounding structures may yield clues. When the tumor extends into the lumen of the bronchus, information may be gleamed as to its exact location, which may be of aid in selecting lobectomy or pneumonectomy as the proper intervention, or in judging operability Christie stresses the necessity for preliminary roentgenography and urges caution that the biopsy specimens be taken from the actual tumor and not from surrounding inflammatory tissue

Diagnosis - Differential diagnosis from bronchiectasis may be almost impossible Pulmonary abscess can be excluded only by bronchoscopy unless the abscess has perforated into the pleural cavity permitting diagnosis by aspiration of pus Dermoid cysts are usually easily distinguished by their smooth outlines and the presence of calcifications and thymoma by the roentgenologic demonstration of its position immediately in back of the sternum and its prompt response to radiotherapy. It must also be kept in mind that the apex may be the site of benign as well as malignant Pneumothorax may also give valuable diagnostic information as regards the presence or absence of adhesions, the location of the tumor in relation to the lobes of the lung and hilar structures, as well as the size of the tumor In a few cases exploratory thoracotomy may be justifiable Craig reports four cases, in which the changes in the bony structures resemble acromegaly in one case and rheumatoid conditions in the others constituted the first signs of pulmonary carcinoma. There was no sign of obstruction of the pulmonary circulation or of toxic absorption.

It is suggested that a routine examination of patients with rheumatism or joint changes of obscure origin might be a helpful aid in earlier diagnosis of lung tumor According to Mosto and Polak, very early in cancer of the lung the sputum contains groups of tumor cells which can be utilized in diagnosis They recommend the histologic examination of paraffin embedded sputum and base their conclusions on the tissular rather than cytologic findings, noting the structural changes and loss of orientation and of polarity of the cells within the group If horny substance is present in the sputum, a further histologic search is indicated Serial sections gave positive results in 685 per cent of cases verified at autopsy Jaquerod draws attention to "crab claw" proliferations seen in the roentgenograms of two cases when exposed at different angles. This picture is present only in the very early stages before any reaction of the lung tissue to the carcinoma has occurred and is analogous to the early picture of breast carcinoma

Prognosis—Prognosis is poor in carcinoma of the lung and the operative mortality rate of pneumonectomy is high. In very early cases, bronchoscopy may be of aid in removal of the tumor or direct application of radium (L. F. Frissell and L. C. Knox¹²). In attempting to ascertain the extent of the neoplastic invasion of the lung tissue with a view to determining operability, Ameuille and Fauvet stress the significance of noncancerous consolidations in cases of pulmonary carcinoma.

dence of consolidation has always been taken as evidence of an advanced stage of cancerous invasion, whereas one has always to consider the possibility of concomitant attacks of pulmonary collapse

Treatment-In their monograph on the Surgical Treatment of Cancer of the Lung, Lambret, Malabray and Driessens mention among the possible interventions partial pneumectomy or lobectomy or total pneumectomy with preoperative phrenic resection, pneumotomy and thoracoplasty They are advocates of the one-stage lobectomy or pneumectomy After a preliminary pneumothorax they catch the pedicle of the lung between two tourniquets, then ligate the lobular and pulmonary pedicle and cover the pedicle with lung tissue Pneumectomy is preferable to lobectomy but has frequently to be supplemented by thoracoplasty Of the 58 cases in their series 25 or 43 per cent were cured, some having been followed up as long as four, five, six and seven years Twelve (207 per cent) diet of recurrence of metastases within 6 to 20 months, six of pneumonia or bronchopneumonia, four of empyema, two of hemorrhage from the costal arteries and the remaining 35 per cent of complications such as embolic myocarditis or septicenna The mortality for lobectomy was 30 per cent and for pneumectomy 50 per cent Chevalier Jackson does not advise removal of malignant tumors through the bronchoscope

R Overholt uses the anterior thoracic incision. He believes that pneumectomy by separate ligation of the hilar structures is valuable because it permits division of the main bronchus close to the carina, removal of the mediastinal glands and because it presents less danger of hemorrhage and air embolism. Where a single lobe or the middle and lower right lobe are involved pneumectomy and lobectomy by mass ligation are ad-

vocated The lower lobes are exposed through a postlateral incision and the right middle lobe through a lateral incision

Among the factors contributing to success in these operations he mentions preliminary pneumothorax, intrapleural thorascopic examination and venous pressure readings for detection of mediastinal metastases He does not make use of phrenic nerve interruption as a preliminary procedure Intratiacheal cylopropane anesthesia was used for all thoracic explorations and oxygen postoperatively in a concentration of 40 to 50 per cent After four to five days this was reduced and the tent used only as indicated Postoperative intrapleural pressure determinations were made after operation and every 12 hours for two to three days, later as indicated If culture of fluid from the chest proves positive the pleural space was drained at once with constant suction and irrigation Tube drainage was applied in all lobectomies. If no infection is present, thoracoplasty may be postponed, otherwise a graded thoracoplasty is indicated. In all Overholt performed lobectomy in 19 patients, two suffering from carcinoma and 17 from bronchiectasis. In this series there was only one fatality In 11 pneumonectomies (nine carcinoma and two suppurations) seven were successful, and four of his pneumonectomized carcinoma patients survived 38, 32, 7 and 4 months respectively

W F Rienhoff, Jr ¹³ describes a new method for closure of the main bronchus during the operation of total pneumonectomy. He has used this method in 23 patients with good results. The bronchus is cut across in the mediastinum near the bifurcation of the trachea. The incision is made slightly oblique to the longitudinal axis of the bronchus on a line running from above and lateral to

below and medial The cut edge of the stump forms an angle of about 45 degrees with the superior border of the primary bronchus and about 135 degrees with its inferior medial border The cut is also made on the bias so that posterio-membranous portion is a trifle longer than the more anterior cartilaginous wall Interrupted fine "a" silk sutures are then placed in the membranous portion in such a way that the needle does not penetrate the lumen but picks up a portion of the tissue a few mm proximal to the cut edge The needle is then inserted into the cut edge of the cartilaginous ring of the bronchus directly opposite including only the tissues that are external to the mucous membrane From 10 to 12 sutures are placed in a fan-shaped pattern. When the knots are drawn the relaxed tough membranous walls are not only nicely fitted to the inner surface of the semicircular cartilaginous ring but also the membranous portion is rolled over the cartilaginous cut edge The cut ends of the mucous membrane are thus approximated on the inside of the blind end stump method tends to flatten out the horseshoe shaped bronchial cartilage rather than constrict it so there is no tension on the suture line

PULMONARY TUBER-CULOSIS

Surgical Treatment

G L Leslie and R S Anderson¹⁴ reviewed the results of treatment of 1124 patients with pulmonary tuberculosis of the adult type admitted to the Michigan State Sanatorium from 1930 to 1934 Of these 80 per cent were subjected to operative treatment. In 473 per cent the process was arrested, favorable results were obtained in 671 per cent, cavity closure was effected in 712 per

cent of all cases with cavity and sputum became negative in 619 per cent of all patients with positive sputum. authors believe that all patients admitted to a sanıtarıum should have collapse therapy except those in terminal stages of the disease, patients with only doubtfully active lesions and patients who refuse such treatment. In noncavernous cases collapse therapy will prevent cavity formation and even in cases with very mild lesions and in more severe lesions without cavitation better results may be obtained by collapse therapy than by other forms of treatment Leslie and Anderson conclude that artificial pneumothorax by itself will give adequate results in only one-twelfth of all patients Alone or in combination with other procedures it may be used in about 50 per cent of all cases Phrenic nerve surgery alone will suffice only in about one-quarter of all cases and may be used singly or in combination with other procedures in about two-thirds of all patients In itself it may suffice for about seven-eighths of the minimal lesions, nearly half of the moderately advanced cases but only 15 per cent of the far advanced cases In conjunction with pneumothorax it will suffice for about one-quarter of all patients Major thoracic surgery excluding pneumothorax and phrenicectomy was found necessary in one-fifth of all patients Thoracoplasty should not be required in more than 10 In the series per cent of all patients under consideration bilateral collapse was done in 160 patients, or 142 per cent of the group By careful selection and timing of the various procedures the necessity for major thoracic surgery is diminished and the results of treatment show improvement in direct proportion to judicious therapy applied in the early stages

C. M. F Sinding-Larsen¹⁵ made a careful study of the results of collapse therapy in 1126 cases of tuberculosis in Denmark at the Veljefjord Sanatorium from 1906 to 1932 Best results were obtained from effective artificial pneumothorax, but the procedure was effective in only 40 of 1021 patients. Seventy-three additional good results were obtained with intrapleural pneumolysis Poor results were believed to be due to the madequacy of the operative procedures Recently the Semb type of operation has been adopted. The author concludes that even with long sanatorium treatment, patients with cavernous lesions have a poor prognosis unless they receive collapse treatment in time and believes that indications for this therapy should be extended

Thoracoplasty - It is only by the careful evaluation of multiple criteria that the decision for thoracoplasty can be judiciously made. The roentgen findings are of great aid, because, as stressed by P D Crimm, D M Short and C S Baker¹⁶ a patient who to all appearances 18 improving may show a very soft infiltration in the roentgenogram, which would contraindicate collapse until resolution and fibrosis are demonstrable Thoracoplasty is contraindicated in early tuberculous infiltration unless bleeding cannot be checked by other means making a choice of the type of operation, one should be guided by the aim of conserving as much normal lung tissue as possible These authors feel that single procedures are often given preference merely because of greater availability, the danger of a poor choice of operation, lying in the fact that there is an optimum period for each intervention oplasty should be used as an early aid to cure rather than as a last resort G Mittermeier¹⁷ stresses the value of supplementary tomography with bacterio-

logic and roentgenologic findings for the demonstration of cavities obscured by adhesions, effusion plugs or oleothorax. Accurate depth localization is possible by this means as well as demonstration of small cavities in the midst of small spotted shadows and information not supplied by ordinary roentgenography. The demonstration of small cavities near the back of the contralateral side might affect the indication for surgical collapse therapy It also permits a postoperative control of results and decision as to whether further correction will be necessary. Tomography permits differentiation of regeneration shadows posterior or anterior to the cicatrice as well as demonstration of a residual cavernous lumen in a plastic cicatricial area Primarily it permits of accurate cavern localization which will determine the type of intervention, differential diagnosis between intrapleural processes and pleural deposits and an accurate analysis of endopleural adhesions

S O Freedlander and S E Wolpaw¹⁸ tested the results of thoracoplasty by comparison of a series of cases thus treated with a group of patients refusing such operation The series included 85 patients and a control of 58 patients The cases of both groups were divided into "good chronics" and "slipping chronics" Without thoracoplasty the course in "good chronics" is very different from that in the "slipping chronics," but thoracoplasty notably improves the prognosis of each group both as regards healing and restoration of working capacity The writers feel that the practice of delaying operation in the good chronic cases in the hope of a spontaneous recovery is unjustifiable.

J. R Head¹⁹ believes that the failure of thoracoplasty to close large apical cavities accounts for many partial successes The results in this group can be greatly improved by using an initial paraffin pack. In a certain number of cases this will close the cavity and render the sputum negative. If it fails to do this, it will nevertheless diminish the size of the cavity and the amount of sputum rendering a secondary thoracoplasty safer and more likely to produce the desired results E S Welles²⁰ also approaches this question of incompletely closed cavities following thoracoplasty The only cases which he feels may be blamed on technic are those in which there has been too long a wait between the stages of the operation Semb apicolysis will not suffice to drop the lung in some cases. Roentgenograms taken immediately before operation may indicate that the cavities have been obliterated, while films taken two or three months later will show them to be open, especially if a Bucky diaphragm is used with over-exposure of the films In such cases, Semb obtained good results in 11 out of 14 by reoperation The author had no success in six cases in which he tried this procedure. The cavities were reduced in size but not closed and he doubts whether reoperation is worth Some cavities simply will not collapse completely owing to quality of their walls and surrounding lung tissue

L A Hochberg and P N Coryllos²¹ contend that the presence of air or fluid in the pleural space defeats the purpose of thoracoplasty. The relative number of poor results is considerably diminished in the absence of pneumothorax at the time of thoracoplasty. He is therefore of the opinion that an effort should be made to transform all existing preoperative pneumothoraces to the least possible volume and if any pneumothorax remains at the time of thoracoplasty it should be aspirated.

H Lilienthal²² recommends conservation of the first rib in apicolytic

thoracoplasty. The artificial space over the tuberculous cavity is packed firmly with crumpled rubber dam, slightly thicker than that used in dentistry, which is held firmly in place by suturing the skin and muscle over it. Three to five days later the sutures and rubber dam are removed. Gauze packing is inserted until firm granulation has taken place after which the gauze packing is discontinued and the soft part of the chest wall will be drawn in The operation may be modified by suturing the wound permanently at operation and leading the end of the drain out through the inferior angle of the wound. This drain may be removed from three to five days after operation and a soft fenestrated tube introduced. Compression pads are applied to the upper chest wall to aid retraction and healing

Extrafascial Apicolysis — This method first described by Carl Semb in 1935, is gaining in popularity both here and abroad Semb is of the opinion that retraction of the lung should be accomplished concentrically in three planes, from the side, from above downward, and from the front backward. It is necessary to mobilize the apex of the lung by extrafascial division of all suspensory ligaments of the apex (which fix the lung apex to the neurovascular trunk, to the vertebral column and to the mediastinum outside of the endothoracic fascia) The ribs must be radically resected and the costal periosteum, the intercostal muscles, the blood vessels and nerves divided, so that these structures are not loosened from the surface of the lung Phrenic exeresis is not used One or more stages may be used according to the condition of the patient The postoperative mortality will be found to be in direct proportion to the number of ribs resected at one time. Not more than three to five should be resected in the

first stage In a few cases it may be advisable to do an extrapleural pneumolysis with radical rib resection first and an extrafascial pneumolysis in one stage later Recently the operation has been done routinely in multiple stages with better results and broader indications. The last 68 patients were operated upon without a death. In 42 of 45 cases of an earlier series the cavities were completely closed and the sputum negative. A negative sputum was obtained in 109 of 147 cases or 75 per cent.

Orientation is fairly easy in this method owing to the wide exposure, the greatest danger being that of injury to the innominate or subclavian veins with subsequent air embolism during denudation and resection of the first rib An abnormally located V intercostalis suprema might also be injured and give rise to air embolism Posterior near the spine, hemorrhage may be produced in attempting to free the intercostal vessels, but can be avoided by double ligation In front the trunk of the sympathetic may be injured (Horner's syndrome). By more cautious staging of the operation the mortality has been reduced from nine per cent to three per cent Also the postoperative reaction becomes increasingly severe with the increasing number of ribs resected Wound infection occurred in ten per cent 23

(oryllos (loc cit) recognizes this technic as a decided step in advance which gives favorable results in 80 per cent of unilateral cases and in bilateral cases renders possible a more selective collapse of the diseased upper lobe as well as limitation of the number of resected ribs. He recommends it for all bilateral cases and in all cases with giant cavities as well as in small cavities limited to the extreme apex.

Likewise R H Överholt²⁴ considers lung mobilization a decided gain. The

extrafascial apicolysis can be carried out at the time of the first stage thoracoplasty and further mobilization may be accomplished at the second stage operation A more effective collapse is obtained and the clinical improvement following the first stage is greater. The first stage leaves all uncollapsed lung below the level of the unresected ribs so that the interval between stages may be lengthened without danger The number of supplementary operations is reduced as well as the average number of stages Overholt bases his report on a series of 233 patients with 573 thoracoplasties done from 1932 to 1935 without lung mobilization and 106 cases up to June. 1936, with combined apicolysis and thoracoplasty The operative mortality in the first group was 64 per cent, although only 15 per cent had active bilateral disease In the latter group 28 per cent had active bilateral involvement with cavitation, yet the operative mortality was only 56 per cent. In the first group collapse was satisfactory in 71 per cent and in the second group in 92 per cent Only 10 to 15 more minutes are required for mobilization of the lung and the routine combination is preferable to thoracoplasty alone in all upper lobe involvements, and especially in bad risk cases In patients with bilateral apical tuberculosis, fewer ribs have to be resected by this method

Technic—First Stage—The usual posterior upper thoracoplasty incision is made and the serratus magnus divided at its point of origin on the ribs, and the longissimus dorsi muscles separated from the posterior angle of the ribs and retracted medially. The posterior half of the third rib, and all of the second and first ribs are resected with the transverse processes of the second and third vertebrae. It is not always necessary to remove the first transverse process.

removal of the ribs and transverse processes of the vertebrae, the mobilization is accomplished as follows (1) ligation and division of the first and second intercostal vessels and nerves, and removal of the first and second intercostal muscle bundles The extreme posterior portion of the lung is then separated from the vertebral bodies, (2) gentle traction on Sebileau's bands with a gauze sponge beneath the hand on the lung The bands are then easily divided beginning posteriorly with the costopleural ligament, then the pleurovertebral ligament, and finally the vertebropleurocostal ligament Care must be exercised not to injure the brachial plexus or subclavian vessels

Second Stage - The second stage must not be attempted until the maximum recovery is attained. It is moreover impossible to evaluate the results of the first stage until a certain time has elapsed, when the roentgenogram becomes clear The latter is often obscured by serum during the first weeks after the first stage Overholt emphasizes the fact that the above down sequence of rib removal permits longer delay and lung mobilization even more A third stage should be planned if more than a safe number of ribs need to be resected at the second stage Four ribs are maximum for resection at any stage. In planning second stage operation, lateral or oblique roentgen exposures are used in addition to ordinary posterior-anterior films

An incision is made in the scar from the first stage, exposing the fourth to seventh ribs throughout their posterior two-thirds as well as the area of previous thoracoplasty. The latter is most important. The serratus magnus muscle is resected from the scar tissue and the additional ribs resected from above downward. The location of the cavities and their size determine the length of rib to be resected, the entire length and cartilage of the first

three ribs being always resected and less from the fourth rib down. The anterior half of the third rib is then removed. this section having been left in situ at the first stage to prevent paradoxical movement of the chest wall The transverse processes of the corresponding vertebrae are then removed After apical mobilization the apical cavities usually are found opposite to the fourth to seventh vertebrae The transverse process must, therefore, be resected close to the body of the vertebrae in order to obliterate the vertebral gutter. Lung mobilization is then completed The chest wall retracts after removal of the ribs but is suspended by scar tissue and the regenerating third The bridge is divided posteriorly down to the endothoracic fascia with ligation of the fourth intercostal vessels and division of the nerve Some of the scar tissue is resected with the fourth intercostal muscle bundle Occasionally the fifth intercostal vessels and nerves are divided to mobilize the posterior border of the lung First stage thoracoplasty gives vertical collapse from above downward, the second stage affords chiefly a lateral collapse of the lung. Closure of the wound is done as in the first stage Drainage is not employed Serum that may have collected is aspirated, with care to introduce the needle at a distance from the incision postoperative care is the same as for the first stage, the patient being instructed to lie over a folded pillow on his operated side If there is paradoxical movement in the chest wall, shot-bags are used

Third Stage—If a third stage is planned, the interval between the second and third stage should be about three weeks so that regeneration of the ribs resected at the second stage will not hinder satisfactory collapse Further surgery following the second stage is not

indicated unless there is definitely demonstrable open cavities. As a rule, resection of one or two ribs will suffice. In a few cases, temporary phrenic nerve paralysis was used to close small persisting cavities, and a third stage thus avoided. If revision becomes necessary, this, too, should be done from above downward and in stages if indicated.

According to J D Steele, Jr, 25 there is rarely an indication for lobectomy or pneumonectomy in pulmonary tuberculosis and the operative mortality of these interventions is high Bronchial stenosis does not necessarily require such procedure as it may respond to thoracoplasty. It is only in cases in which thoracoplasty is contraindicated or does not offer hope of improvement that lobectomy or pneumonectomy might be tried

Intrapleural Pneumolysis

I W Cutler²⁶ estimates that this piocedure can be employed advantageously in 20 to 30 per cent of the tuberculous patients in whom pneumothorax can be established, but warns against operating during the first two or three months of a pneumothorax, against delaying operation more than four to six months, and against attempting too much at one cutting. He advises that a phrenic nerve operation be done to support the contralateral lung, if actively diseased, or a partial pneumothorax instituted before beginning pneumolysis Not all adhesions or even all of one adhesion needs to be severed to close a cavity believes that complications may be largely avoided by the adoption of the single cannula technic, and the use of electrosurgery instead of galvanocautery Among the complications may be mentioned spontaneous pneumothorax, pleural reactions, tuberculous empyema, hemorrhage and the loss of pneumothorax space By the author's method, all instrumentation is through an opening in the chest in the second anterior interspace, and the instruments have been so improved as to meet almost every mechanical problem. The most important instrument is the Cutler operating forceps thoracoscope by means of which the adhesion can be grasped and held until coagulated and resected. There is also a diagnostic transilluminating telescope, a thoracotome and curved electrodes for short adhesions.

According to Steele (loc cit), onefourth of ineffective pneumothoraces can be rendered effective by intrapleural Although Diash has repneumolysis ported 200 personal cases without a fatality, it must be admitted that the operation is not without danger. Massive fatal hemorrhage may occur and the surgeon in attendance should always be ready to resort to an emergency thoracotomy Regarding the relative value of the closed and open intrapleural pneumolysis, R S Anderson and J. Alexander²⁷ state that the advantages of the latter consist in better orientation and more satisfactory examination of the adhesions from all angles, as well as better control of bleeding The disadvantages mentioned include the difficulty of maintaining pneumothorax and the higher operative mortality, so that the open method is recommended only in cases in which the adhesions could not be divided by the closed method Leslie likewise prefers the closed operation but adds that an open intrapleural pneumolysis is better than making no attempt whatsoever If thoracoplasty is not contraindicated, it is preferable to open pneumolysis Anderson and Alexander (loc. cit) conclude that open intrapleural pneumolysis should be attempted only in patients in whom the closed method has been tried and in whom thoracoplasty is contraindicated chiefly because of advanced contralateral involvement, and in whom open operation offers the only chance of recovery

Extrapleural Pneumolysis

Steele (*loc cit*) stipulates that the usefulness of extrapleural pneumolysis is limited to cases failing to respond to phrenic paralysis and pneumothorax, and in which thoracoplasty is contraindicated. It may be very beneficial also in certain bilateral cases.

Head reports improvement in his series treated with extrapleural paraffin pneumolysis but no cures W Graf²⁸ used extrapleural pneumolysis followed by repeated air refills in 107 cases There were seven postoperative deaths Complications included necrosis following division of the adhesions, wound infection and late perforation of the lung due to increased pressure Encouraging results have also been reported by J E H Roberts²⁹ with this method

PHRENICECTOMY

A complete review of the history, effects and technic of this method has been made by A H Aufses 10 on the basis of a collection of 17,570 cases from the literature Whereas in some clinics phrenicectomy is being used less and less, in others it is still almost a routine procedure Only the adult type of tuberculosis with cavitation and fibrosis The best results responds favorably are obtained in cold, afebrile cases in which the process of cavitation is very slow or stationary Although lower lobe lesions are best suited for this therapy some good results have been obtained also in cavities of the upper lobe Phrenicectomy may be beneficial on the more active side in bilateral involvement. It is contraindicated in emphysema and myocarditis owing to dyspnea There are few other contraindications and the method may be considered as a minor surgical procedure. Among complications that have been reported may be mentioned injury to the thoracic duct, to the cervical sympathetic, the bloodvessels and pleura, as well as atelectasis and pneumonia. Less common complications include massive collapse, contralateral exudative pleurisy, pulmonary edema, hemoptyses, cardiac failure and miliary dissemination of the tuberculous infection. In some cases what is known as the Roemheld complex may appear with vomiting, nausea and tachycardia Cardiospasm has also been reported.

In 10,567 operations performed as independent procedures cure was obtained in 23 3 per cent

D A Cooper and W H Erb31 have collected 46 fatal cases from the literature, thus bringing the mortality rate up to 05 per cent. It seems that by far the largest number of these deaths are due to spread and aggravation of the tuberculous process Phrenicectomy is definitely contraindicated in the presence of cardiac disease Epstein's contraindications to phrenicectomy are cited as follows: (1) definite exudative type, (2) dissemination of process to both lungs, (3) hematogenous forms of tuberculosis, and (4) old cases of fibrocavernous tuberculosis with extensive limitation of contractility of the lung and secondary cardiac insufficiency emphysematous hearts there is always danger of right-sided heart failure Careful observation of the patient during the period between injection of the anesthetic and isolation of the nerve is recommended and if unfavorable symptoms develop during this period further surgery should be avoided It is a good precaution to produce a temporary paralvsis of the nerve with novocaine and then determine the vital capacity of the patient or observe how long the

patient can hold his breath Normally he should be able to hold his breath for 50 to 70 seconds. In doubtful cases a two-stage procedure may be used the first stage consisting in exposure and injection of the nerve with novocain, resection of the accessory nerves and application of a black silk ligature about the nerve. The wound is closed with adhesive bands and the patient observed for 24 hours, after which the operation may be completed in a second stage if no untoward symptoms have appeared

- L S T Burrell³² lists the indications for evulsion of the phrenic nerve as follows
- 1 To relieve symptoms such as dry cough due to diaphragmatic irritation, vomiting after meals or persistent hiccup
- 2 When there are unilateral fibrosis and displacement of the mediastinum. After completion of pneumectomy, phrenic evulsion is indicated if there is much displacement of the heart and mediastinum
- 3 To give additional rest to the lung when artificial pneumothorax has failed It is more valuable in basal than in apical cases
- 4 As a preliminary to thoracoplasty unless only an upper thoracoplasty is contemplated
- 5 As an aid to artificial pneumothorax if the lung is adherent to the apex and diaphragm. If adhesions are present that cannot be cauterized, phrenic evulsion should be practiced to relieve the pull of the lung on them and is thus definitely indicated in a so-called suspended cavity, where it will help to prevent rupture of the lung.
- H G Trimble and B H Wardrip³³ recommend combination of pneumoperitoneum with phrenic nerve paralysis, asserting that by addition of the subphrenic pressure exerted by the pneumoperitoneum, the paralyzed diaphragm

may rise sufficiently to reduce lung volume by two-thirds, the elevation being twice that obtained by phrenic paralysis alone. Such a measure is advised in patients in whom pneumothorax is contraindicated owing to adhesions and in patients with bilateral lesions who could not tolerate a bilateral phrenic paralysis

B P Potter, F B Berry and F Bortone³⁴ present a five-year study and follow-up of phrenic interruption in the treatment of *pulmonary tuberculosis* in a series of 95 cases under observation for from one to five years, following operation

In 68 cases the operation was used as an independent procedure, in 12 as a supplement to insufficient pneumothorax and in 15 for miscellaneous reasons Among the contraindications are mentioned huge cavities, thick-walled cavities and cavities embedded in fibrous infiltrate, peripherally located cavities, lesions within a lung surrounded by a thick pleura and multiple cavities Best results are to be expected in small or moderate sized caveinous lesions with a surrounding zone more or less free of infiltrate A cavity within a shrinking lobe may be treated by this method if the infiltration is not too extensive and provided the cavity has been decreasing in size along with contraction of the lobe From phrenic evulsion as an independent procedure, closure of the cavity may be expected in many cases and clinical improvement sufficient to permit thoracoplasty in some cases A favorable response may be obtained also in persons in whom pneumothorax was impossible or failed As a supplement to ineffective pneumothorax phrenicectomy should be used only if pneumolysis is definitely contraindicated or inadvisable following thoracoscopy and for adhesions of the nature described in particular when they suspend a partly collapsed lung to the apex and diaphragm In the presence of extensive adhesions to abandon the pneumothorax for a thoracoplasty or to supplement it with one

In 38 cases in which phrenicectomy was used an independent procedure closure of the cavity was obtained in 47 per cent and reduction in the size of the cavity with general improvement in 31 per cent Thoracoplasty was avoided by this operation in 15 per cent. The average interval between the operation and closure of the cavity was seven and one-half months In no case in which the intervention failed was the opportunity for thoracoplasty lost Success may be expected in about 50 per cent of the cases in which the measure is used as an adjunct to pneumothorax The principal indication for phrenic interruption for miscellaneous purposes is for reduction of the intrapleural space Temporary phrenic paralysis is just as revocable an operation as pneumothorax and should be tried before the latter as it is a much simpler procedure

G L Leslie and R S Anderson³⁵ used phrenicectomy as an independent procedure in about one-quarter of their patients They found that it will suffice for seven-eighths of the minimal lesions, nearly half of the moderately advanced cases but only for 15 per cent of the far In combination with advanced cases pneumothorax phrenic surgery will suffice in approximately one-quarter of all patients In pneumectomy and lobectomy the use of preliminary phrenic paralysis appears to be losing in popularity

F R Harper³⁶ found that a combination of pneumothorax and phrenic interruption could be expected to close 80 per cent of cavities failing to respond to either method alone Sputum became negative in 89 per cent of cases so The incidence of pleural effusion was diminished and the intervals

between refills of the pneumothorax could be lengthened.

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THYROID SURGERY

By GILSON COLBY ENGEL, M D.

THYROIDECTOMY

A S Jackson1 draws attention to the fact that whereas not so long ago cases of hyperthyroidism were overlooked until the moperable stage, there is at present a tendency to rush patients to operation without proper indication. Many functional conditions are being diagnosed as A recent survey of hyperthyroidism 100 cases shows the following conditions diagnosed as hyperthyroidism Nervous exhaustion, physical exhaustion, menopause, colloid goiter, septic tonsils, and psychosis Jackson emphasizes the fact that the metabolic rate must not be taken too literally, but must be evaluated on the basis of repeated tests and a consideration of the attitude and condition of the patient at the time of the test. In doubtful cases an iodine test may be of value, since a negative result will exclude exophthalmic goiter provided the patient is not iodine-fast A sensation of constriction in the neck and of choking are not symptoms of goiter but only of nervous tension, which requires a change in environment and not removal of the gland

Treatment of hyperthyroidism is of great importance in avoiding unnecessary thyroid surgery A prolonged stay in bed is not indicated except in cases of serious cardiac involvement administration of iodine will only increase the operative risk but iodine must be given preoperatively in all cases of hyperthyroidism Better results are obtained if cervical nerve block anesthesia and mild sedatives are employed After operation 200 drops of iodine should be administered daily for a short time, and subsequently small amounts for a period of about six months Many useless thyroid operations may be avoided if these points are observed

A S McQuillan and L Breidenbach² report their results in operations for goiter in a series of 803 cases which were followed up from six months to 14 years They found postoperative thyrotoxicosis to be the most frequent cause of death Eight of the 30 patients with this complication in the present series died Recurrence of the goiter after operation will depend upon the careful supervision and mode of life for a period of two years following operation suffices to leave a portion of the thyroid equal to about one-fourth of normal lobe on each side Mild temporary hypothyroidism persists for a few months after operation in successful cases There were 54 recurrences in the present series Further treatment was successful in 18 of the 33 cases in which the primary operation was performed by the authors Most recurrences take place during the first or second year after operation A temporary recurrence may be due to emotional or physical strain and will disappear on removal of the cause In 28 cases the thyrotoxicosis persisted after operation, 15 having a long history of thyroidism and prolonged iodine administration but adequate removal of gland tissue, whereas the rest showed inadequate operation Exophthalmos persisted in 42 cases, and there was cardiac involvement in 43, usually auricular fibrillation Thirteen were cured of the heart condition by operation, 20 showed improvement and ten remained unimproved, or grew worse. Parathyroid tetany developed in two cases and there was one case of true postoperative myxedema Postoperative pneumonia occurred in nine cases with five deaths, and embolism in six cases with five deaths Tracheal collapse occurred in five cases The latter may be prevented by the use of intubation anesthesia The laryngeal nerve was injured in 18 cases but function was completely restored in all except two Hemorrhage was observed three times during operation due to slipping of hemostats or For this reason the authors advocate clearing the field of hemostats and using transfixion ligatures for the larger vessels Drainage was established in all cases, and the drains removed after 12 to 48 hours Infection developed in 12 cases, the worst case being one in which silk sutures were used authors have discontinued the use of silk, preferring catgut for sutures, although W B Parsons, in discussion, insists that progressive improvement in statistics has been noted annually at the Presbyterian Hospital since silk has been used as suture material. The silk must be extremely fine but affords better hemostasis, less tissue reaction and cleaner healing

Psychosis developed as a postoperative complication in 0.7 per cent of the above series. The high mortality of cases complicated with diabetes has been considerably reduced since introduction of iodine plus insulin and stage surgery. Coma may develop following operation in cases with unsuspected diabetes. For

this reason it is advisable to study the carbohydrate metabolism in all patients with hyperthyroidism and glycosuria or acetonemia, the latter being occasionally associated with thyroid toxemia.

W P. Kroger and C G Toland³ likewise find the most frequent cause of death to be postoperative hyperthyroid-15m Of 11 deaths due to this cause, six might have been prevented if the usual preoperative treatment had been prolonged or if a multi-staged operation had been used All of the 25 fatal cases in the series with two exceptions had single stage operations. There is no way of predicting a dangerous postoperative crisis Clinical impressions are the best guide in this respect, tachycardia being the best single sign of hyperthyroidism Mental instability and emotionalism are danger signs The basal metabolism is not a reliable criterion

A Atnan, E Fenz and K Uıberrak4 claim that the blood sugar takes a peculiar course after thyroidectomy hyperglycemia falls, not as usual after three to five hours, but remains high for as long as 24 hours or rises repeatedly This has been explained as the result of surgical trauma and the fever, sweats, tremor and tachycardia may also be due to this In two cases the iodine content had almost doubled after operation on the thyroid Whereas following other operations, the blood cholesterol is only insignificantly or not at all reduced, after thyroidectomy for Basedow's disease, the cholesterin in one case disappeared entirely except for tiny traces and was considerably below that recorded in other operations also in the remaining cases

G Crile and G Crile, Jr,⁵ discuss hyperthyroidism in children under five years of age, which is so rare as to be a curiosity, the incidence being about one in 6670 cases. They report four cases

among the 26,682 thyroid patients at the Cleveland Clinic, three of which recovered after thyroidectomy and one after conservative therapy Thyroidectomy is the treatment of choice and should always be done if exophthalmos is progressive. The dangers of operation are no greater in children than in adults, and the authors have experienced no fatalities in their last 40 thyroidectomies in children under 14 years of age The most common cause of death following thyroidectomy is thyroid crisis, other causes including pneumonia, and cardiac failure A one-stage thyroidectomy can usually be done without great risk

F A. Coller and A M Boyden⁶ trace the development of the technic of thyroidectomy and describe the method used at the University of Michigan Hospital, including a special method of dealing with the superior pole, somewhat like that of Eades The zipper sheet is used for draping and following a Kocher incision, the platysma is divided transversely The superficial blood vessels in the subcutaneous fat and platysma are coagulated by means of a Bovie unit This will prevent collection of serum beneath the flap and saves time The upper flap of the skin and platysma are dissected upward with minimum bleeding by means of a piece of gauze over the gloved finger, and then retracted with a Murphy rake, the lower flap and jugular veins being unmolested The deep cervical fasciae are then divided in the midline and the sternohvoid and sternothyroid muscles separated and retracted laterally with the cervical fascia by means of a Brewster retractor If indicated, the muscles may be divided transversely. The suspensory fascia of the thyroid are then divided, exposing the upper tracheal rings pyramidal lobe is present it may then be freed The cricothyroid space is defined

by blunt dissection, and the superior thyroid vessels on the anterior surface of the pole are divided between clamps. The pole is then delivered by dislocating it from its bed and pulling it anteriorly. In the meantime the lateral vein is divided. If this dissection is done directly beneath the fascial covering, injury to the laryngeal nerve may be avoided. Only the superior thyroid vessels are included in the hemostats, the upper pole being delivered as a whole

After freeing the normal cervical attachments, the lower pole is easily delivered The isthmus is dissected in its entirety from the trachea in the areolar plane lying between these structures This affords less chance for adhesion of the trachea to the prethyroid muscles and is less productive of tracheitis than if thyroid tissue is left on the trachea Only a small fraction of the gland is left in situ Hemostasis is accomplished by means of catgut ligatures and sutures, as silk sutures were found to offer no real advantage and to be too time consuming Drainage was established in nearly all cases, the drains being removed in from 6 to 12 hours Midline drains should be avoided owing to poor cosmetic results In suturing the sternothyroid muscle, the deep fibers of the muscle are approximated without tension in order to close more completely the dead space left by removal of the thyroid lobes. This procedure is especially useful in substernal goiter to obliterate the cavity that usually fills with serum and blood

C G Heyd describes a simplified procedure for thyroid exposure ⁷ Instead of incising the cervical fascia in the midline and then dividing the ribbon muscles on each side between the upper and middle thirds, he divides both lateral groups of the ribbon muscles between

two clamps, thus giving a larger and The operative more ample exposure field is then minus two clamps that make progress more difficult. The patient is placed in a semi-sitting position with his shoulders resting on a sandbag, and his head extended The hook retractors placed under each clamp are removed after resection of the thyroid, and the muscle groups approximated and united by three interrupted sutures of No 1 chromic catgut This procedure will also lessen the actual time of operation and expedite healing Serum collection beneath the skin is less frequent by this method and the neck regains its normal shape more rapidly

M Nordland8 emphasizes the fact that injury to the recurrent laryngeal, to the parathyroids, and hemorrhage may best be avoided by careful hemostasis as injury to the two former occur chiefly during attempts to ligate the thyroid arteries or to control hemorrhage within the capsule He applies a ligature to the inferior thyroid artery before proceeding to excision of the gland, using a linen suture after resection of the gland, ligature is rarely applied to the trunk of the artery but more often to its branches, thereby increasing the danger to the recurrent laryngeal nerve and providing inferior hemostasis Before mobilizing the lobe, after grasping it firmly with the tenaculum, it is well to apply ligatures or clamps to the middle thyroid veins and cut between With this vein bisected mobilization is more complete The superior pole is next ligated by passing a carrier from within outward to include the pole en masse or the artery alone, as desired The ligature must pass around the whole pole and not through it A similar ligature is applied to the inferior thyroid veins directly below the lower pole The gland can then

be resected with very little bleeding During resection of each lobe, an assistant holds a finger under the external row of forceps to help control bleeding After the capsule of both lobes has been sutured the wound is held wide open and the patient asked to strain to expose hidden bleeding points. Ligation of the superior thyroid arteries has splendid results in cases which fail to respond to Lugol's solution in preparation for thyroidectomy

M. Davison and L J Aries9 conclude from their careful observation of 100 consecutive patients subjected to bilateral subtotal thyroidectomy that if sufficient gland has been removed and the patient has received adequate preoperative treatment there is no rational basis for the use of postoperative iodine Untoward reactions following this operation are properly treated by dilution of the thyroxin in the circulating blood stream by administration of enteral or parenteral fluids The use of iodine postoperatively is still indicated in incomplete operations where residual thyroid tissue has been left in situ requiring iodinization as a protective measure

The same authors9 recommend twostage lobectomy in the poor risk patient with thyrotoxicosis This operation was performed in 35 of 36 thyrotoxic patients who were considered unfit for bilateral subtotal thyroidectomy Thirteen of these patients refused subsequent operation following the primary lobectomy because of the marked improvement in their condition After primary lobectomy the basal metabolic rate fell from 585 per cent to 26.8 per cent The postoperative course was milder than that observed in a good risk patient following bilateral subtotal thyroidectomy Two-stage lobectomy may replace polar ligation in the treatment of poor risk patients

Thyroidectomy in Heart Disease

It is generally agreed that improvement in results from this intervention depends largely upon a proper selection of patients In his schematic drawing demonstrating indications for various procedures in the treatment of coronary diseases, A Ochsner¹⁰ presents the type for thyroidectomy as one with some fibrosis of the cardiac muscle and occlusion of the coronary arteries of thrombotic rather than vasomotor origin, the angina being one of effort rather than of emotion M Dinnerstein, C Weeks, O Woodruff and A R Tillev¹¹ perform total thyroidectomy only on such patients as suffer attacks of precordial pain regularly after a definite amount of exertion, and in the so-called decubitus cases, in which the patient is unable to walk more than a block without suffering an attack Patients with irregulai attacks or signs of progressive coronary disease are excluded, as well as those exhibiting neurotic or nervous symptoms Cases of cardiac decompensation are considered for thyroidectomy only if they have received treatment over a long period (nine months to six years), and the operation is done at a time when the congestive failure shows improvement following treatment. He obtained his best results in the slowly progressive or stationary types Patients with active pathologic cardiac processes are excluded, as also those giving evidence of active rheumatic processes or syphilitic heart disease R Singer¹² believes that thyroidectomy is indicated in cardiac defects and hypertension with chronic decompensation, in which digitalis or strophanthin give poor results Cases of refractory dyspnea will often respond to this operation, and good results may also be expected in angina pectoris and obliterating endarteritis Operation is contraindicated in cases in which the basal metabolism is below normal

Nelson M Percy¹³ offers the following suggestions as an aid to diagnosis of thyrocardiacs auricular fibrillation. decompensation, failing health in the middle-aged to elderly patient obviously not due to another condition, and goiter consciousness Diagnosis may be confirmed by bed rest, metabolism determination and response to cardiac and W H Parsons and iodine therapy W. K Purks¹⁴ emphasize the fact that thyroidectomy is a symptomatic treatment which does not alter the cardiac pathology and merely substitutes one disease for another They tabulate re-Information as to sults in 362 cases complications revealed tetany in 103 per cent of 281 cases, with one fatality and injury to the recurrent laryngeal nerve in 82 per cent In 229 operations for congestive heart failure the mortality rate was 1048 per cent, with excellent results in 3463 per cent, moderate improvement in 2878 per cent, slight improvement in 292 per cent and no improvement in 33 65 per cent angina pectoris the mortality rate was 375 per cent, with excellent results in 55 46 per cent, moderate improvement in 28 12 per cent, slight improvement in 38 per cent and no improvement in 125 per cent Although the operation will not always prolong life, it may render the time left to the patient more endur-Best results may be expected in angina pectoris. One may reckon with a 50 per cent chance of satisfactory improvement in congestive heart failure, and a 75 per cent chance of success in angina pectoris Lahey regrets the fact that proficiency in this operation is so difficult to achieve owing to the scattered cases presenting proper indications He believes that the indications for this intervention, which has the disadvantage of producing myxedema, will gradually diminish and that it will be used only occasionally in well selected cases Many surgeons are convinced of its value

In order to exclude the disadvantages of the operation, the Vienna Clinic is investigating to what extent subtotal resection might produce the same therapeutic result without myxedematous complications According to Singer (loc cit) the symptoms of myxedema developing in some patients are mild and disappear spontaneously after one or two months

Dinnerstein (loc cit) uses cervical block anesthesia Before proceeding to operate, he makes sure that at least one vocal cord is intact and also makes a careful search for aberrant thyroids In only one case did a severe anginal attack occur during operation After operation, there is usually a mild tracheitis and dysphagia for two to three days There were no postoperative pulmonary complications and tetany developed in only two cases, and was easily controlled by viosterol and calcium lactate Myxedema developed from four to eight weeks after operation, being of insidious onset and varying degree The basal metabolism begins to drop during the second week after operation, falling without treatment, to - 30 to - 40 in five to six weeks The surgical myxedema was not always coincident with the drop in metabolism In patients with myxedema and a normal basal metabolism hypercholesterinemia was demonstrated and for this reason considered to be a better index of myxedema than the basal metabolic At the end of the fifth week. Armour's thyroid extract is administered in doses of ½ grain (0016 Gm) daily Thyroid extract should be given

only in small doses as anginal pain has been known to follow larger doses In the congestive failure group, the basal metabolism averaged — 14 per cent, the blood cholesterol 356 mg per cent per 100 cc, while in the angina group, the basal metabolism averaged - 16 per cent and the blood cholesterol 310 mg per 100 In reply to a questionnaire sent out to 26 clinics, the operative mortality was found to be 69 per cent Eighty per cent of the cases of congestive heart failure were benefited and a much larger percentage of angina Dinnerstein reports two operative deaths in his series of 16 cases of congestive heart failure, and one death in five cases of angina pectoris. The other four showed marked improvement with relief of pain Occasionally pain recurred in a mild form in cold weather or after exertion, but never in a severe enough form to require nitroglycerine One patient was incapacitated by postoperative polyneuritis which is a rare complication In two such cases occurring in the present series, three to six months after operation, thyroid medication brought no relief and calcium and viosterol were likewise without effect An attempt is being made to influence this complication by administration of vitamins

The mechanism of the relief of pain following total thyroidectomy is explained as an injury to the superior and middle cardiac nerves and nerve plexuses on the posterior surface of the thyroid and its vessels. This interpretation of A. A. Weinstein and H. E. Hoff¹⁵ has been refuted according to Ochsner by Langley and Ranson, who state that the superior cardiac nerve contains no cardiosensory afferent fibers. Levine explains the relief of pain as due to a diminished sensitivity to epinephrine

CARCINOMA OF THE THYROID

In a compilation of statistics on 737 cases of malignancy of the thyroid gland encountered at the Mayo Clinic from 1907 to 1936, C W Mayo¹⁶ calculates that malignancy occurs in more than three per cent of adenomatous goiters Nearly half of the cases of carcinoma developed in adenomas and about one-third of the carcinomas were of the papillary type The latter has the best prognosis, especially if associated with adenoma value of Broder's method of grading malignancy was definitely established, regardless of the type of malignancy The best method of treatment was a combination of surgery and irradiation when possible

According to G Crile and G Crile, Jr, 17 malignant adenoma constitutes the bulk of potentially curable malignancies, being nearly five times as common as the papillary type As the histological type cannot be determined preoperatively, any malignant tumor should be dealt with as an adenoma until proved otherwise Since resection of the venous channels draining the affected lobe eradicates the most common site of recurrence, both distant metastases and local recurrences may be diminished if the veins are resected along with the tumor mass High, wide transverse incision is made at the level of the oricoid cartilage The skin flaps are dissected upward and downward to permit separation of the pretracheal fascia and muscles in the midline for examination of the thyroid gland One must proceed gently so as not to rupture the capsule of the gland If the tumor is found to be malignant, the skin incision is extended vertically from the midpoint of the lower flap to the suprasternal notch. The skin flap and subcutaneous fat are then dissected

free of platysma and the deep cervical fascia on each side are retracted pretracheal muscles are separated in the midline from the thyroid cartilage to the suprasternal notch The muscles and cervical fascia on the side of the tumor are clamped and divided transversely as high as possible, exposing the superior pole The sternomastoid, the pretracheal muscles and the cervical fascia are again clamped and divided transversely just above the insertion of the muscles into the sternum A careful attempt is then made to separate the muscles from the underlying capsule of the thyroid and carotid sheath If these are adherent, it is best not to attempt a separation, but to connect the lateral ends of the two transverse incisions by a vertical incision exposing the jugular vein and resect the overlying muscles along with the lobe of the thyroid The internal jugular vein is then isolated, ligated and severed above the point of entry of the superior thyroid vein The inferior thyroid vein is likewise ligated and severed as far as possible from the tumor The inferior thyroid vein and internal jugular with the superior and midline thyroid veins are then dissected out and resected along with the entire affected lobe of the thyroid No attempt should be made to isolate or preserve the recurrent laryngeal nerve as unnecessary manipulation may lead to dissemination of tumor cells. A slight hoarseness signifies little in comparison with a return of the tumor. It is advisable to ligate the arterial blood supply of the thyroid before liberating the gland from the trachea The 1sthmus 1s then divided and the affected lobe carefully dissected free from the trachea sharp dissection gives best results this way the capsule is not broken by hemostats or traction clamps and the gland can be rotated by introducing the finger behind it In bilateral involvement, bilateral ligation of the internal jugular should not be performed at the same operation. Only a small minority of patients are seen early enough to permit complete excision of the tumor. Even if complete excision is impossible, it may still be of value to ligate the jugular vein, excise as much as possible of the tumor, implant radon seeds in the rest, and treat with deep roentgen rays.

As more than 90 per cent of thyroid malignancies have their origin in preexisting adenoma, a prompt and complete removal of adenoma may prevent malignancy Operation is indicated in adenoma as soon as diagnosis has been established One has, however, to distinguish between diffuse adenomatous goiter and discrete adenoma of the thyroid In the former, the entire gland is composed of many small nodules, presenting an adenomatosis In these cases, thyroidectomy is unnecessary but they should be kept under observation If the goiter consists of a single discrete adenoma, or even several discrete nodules, there is a definite tendency to malignancy and radical removal is indicated In patients over 40 years of age, a history of recent enlargement of pre-existing goiter and the finding of a stony hard uncalcified tumor in one lobe is indication for radical excision of the affected lobe and its venous tributaries Calcified adenoma may prove confusing but rarely enlarges so rapidly and can moreover be demonstrated by roentgen ray Chronic thyroiditis is occasionally mistaken for cancer, but tenderness of the gland, pain on swallowing, and the relatively small size of the tumor will clear the diagnosis

Palliative procedures are indicated in the presence of extensive bilateral invasion of contiguous structures Extracapsular extension may be detected by paralysis of one or both vocal cords before operation. In the Cleveland Clinic no case of cure has been known to occur in the presence of preoperative laryngeal paralysis Pain is also an unfavorable prognostic sign and no permanent cures have been obtained in patients who complained of pain. Pain signifies an invasion of the capsule and cervical plexus. Another symptom denoting extracapsular extension of the tumor is fixation of the growth In the presence of these symptoms or with metastases to the lungs or bones radical removal of the growth 18 useless In an effort to render the patient more comfortable, an attempt at palliative treatment with irradiation may be tried. Transverse division of the preglandular muscles may help to relieve pressure on the trachea. Biopsy should always be done to rule out atypical thyroiditis In some cases tracheotomy has to be done as an emergency operation, but this operation is fraught with a high mortality rate, especially in the presence of pulmonary metastases Prognosis in malignant adenoma and papillary carcinoma is fairly good in cases in which complete excision is possible. In a small group of cases in which the jugular vein was excised with the tumor, the prognosis was excellent Papillary carcinoma have a better prognosis than other types

Of 49 cases of malignant adenoma, statistics at the end of three years showed 43 per cent alive and 55 per cent dead from cancer. At the end of five years, 35 per cent were alive and 61 per cent dead of cancer, at the end of ten years, 68 per cent dead of cancer, and after 15 years, 70 per cent dead of cancer.

Of 14 cases of the papillary type, 64 per cent were alive 3 to 14 years after operation. Resection of the veins is not necessary in the papillary type as extension into the veins does not occur in it. However, it is impossible to differentiate preoperatively between malignant adenoma and papillary carcinoma, so it is

wisest to proceed as for malignant adenoma and resect the veins.

E. Haas¹⁸ states that whereas cures are not uncommon in true cancer of the thyroid, they are almost unheard of in malignant adenoma Life may be prolonged by irradiation and operation, but the patients are not cured Excluding sarcoma, malignant adenoma constitutes the most hopeless of all thyroid tumors in spite of its apparent response to treatment and slow course In some cases malignancy in these cases is discovered by symptomatology due to metastasis before the presence of the primary tumor has been suspected

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VASCULAR SURGERY

By GILSON COLBY ENGEL, M D

Embolectomy

The condition giving rise to necessity for this operation is the lodging of an embolus in the arterial tree, which may, according to V H Riddell,1 have its source in the pulmonary veins, a vegetation on the mitral valve, a mural thrombus in the left auricle, an atheromatous plaque in the first part of the aorta, or by way of the systemic veins and a patent interauricular septum. If the embolus passes the aortic bifurcation, which is usual, it may lodge in the iliac vessels but is more likely to reach the termination of the femoral artery The termination of the popliteal artery is the last site of impaction Embolism may occur into the arms, especially the left arm, but these cases are much less numerous In the arm the embolus most frequently

lodges at the termination of the axillary or brachial aitery

The most characteristic symptom is intense agonizing pain, but this may not be present in all cases and may also in some instances be more gradual and less severe This is followed by ischemia and paralysis of the limb The most reliable localizing sign is the site of cessation of pulsation which can be located by palpation and auscultation If operation is done within ten hours of onset, it has almost an even chance of survival Other factors playing a part in prognosis include the source of the embolus, because, of course, in cardiac disease the patient's general condition will be less favorable and there is more danger of recurrence of the embolism The site of impaction is also of some prognostic significance, the outlook being poor for patients with embolus at the aortic bifurcation and better in cases where the embolus has lodged in the common femoral Complicating arterial disease would also exert an unfavorable influence. As a rule, prognosis is better in embolism of the arm than of the leg and naturally the accessibility of the vessel would contribute to the success or difficulty of the operation.

Treatment—Local anesthesia is recommended. If the patient is seen very shortly after the obstruction, it may be possible to milk the embolus into a subsidiary branch. The operation should preferably be done within six hours of onset. If the site of obstruction is easily accessible, a direct embolectomy at this site is indicated with repair and closure of the artery by the classical method (Figs. 1 to 7) or by ligating the artery without resuturing the wound. If the site of embolism is inaccessible, an indirect embolectomy is required with arteriotomy distal to the obstruction.

Incision is made in the line of the artery and the adventitia removed, producing simultaneously a periarterial sympathectomy (Figs 1 and 2) The incision should be below the level of the embolus The clot is then milked out. the wound being saturated with sodium The upper sling is citrate (Fig. 3) loosened and if the blood escapes in jets corresponding to the cardiac beats, the lumen above is clear. If the blood does not escape in this manner, there may be an obstruction higher up requiring another arteriotomy (Fig 4) The collateral circulation is tested by loosening the lower slings with the upper slings tight (Fig 5) Retrograde bleeding indicates free collaterals If this is not present, the incision must be extended downward with injection of saline or aspiration (Fig 6) Finally, the artery is sutured

with a fine needle and oiled silk. The lower sling is removed first to prevent pressure on the line of suture when the blood flows through (Fig. 7). Following the operation, the patient should lie with flexed hip to relieve tension on the artery. In the smaller arteries, secondary thrombosis will often obliterate the lumen. It is therefore better to ligate the artery, which procedure is also safer in the upper limb. In cases of embolism at the

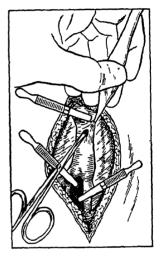


Fig 1—Removing the adventitia (Courtes) Proceedings Roy Society Med April, 1937)

aortic bifurcation abdominal section is contraindicated and the embolus should be removed by retrograde methods after bilateral control of the femoral arteries The author suggests that on one side at least the probing be done through an arteriotomy above the level of Poupart According to Riddell, embolectomy is definitely worth while as it affords a 40 per cent chance of survival as opposed to a 90 per cent chance of developing gangrene if the patient is not operated upon This operation also re-establishes collateral circulation by removing secondary extensions of the clot Even if amputation should be unavoidable, the terrible pain is relieved, and the amputation can be

made lower than would otherwise be possible Of the 20 embolectomies performed in England to date, only 11 were successful C. C Lund reports a series of 25 embolectomies with a mortality of 44 per cent He concludes that quite good results may be expected in embolism of the leg if operation is per-

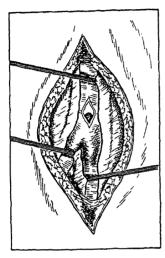


Fig 2—The incision, placed mainly proximal to the embolus. The sling controls held firm (Courtesy Proceedings Roy Society Med April, 1937)

formed early, but that no benefit is to be gained by operation on the arm, although embolism of the arm very rarely leads to gangrene. Cases without embolectomy nearly all died regardless of whether gangrene and amputation followed. In recent articles by Swedish authors, it has been shown that from the time of discharge one-fourth of the patients will die during the first year, one-fourth within the first three years, at the end of five years one-third will still be alive and at the end of ten years, one-eighth. For this reason, Lund feels that the end results justify this intervention.

R R Linton² presents a series of 44 acute peripheral occlusions Embolectomy was performed in 12 cases Four, or 33 per cent, of the extremities were

saved in this group Operation should be done within six hours of onset and is more likely to succeed in patients under 50 years of age in whom the arteries are not calcified. The use of the negative-positive pressure treatment gave best results, being successful in 60 per cent of cases. Linton believes the ideal treatment to consist in a combination of embolectomy followed by pressure treatment and peripheral vasodilatation.

Arteriectomy

R Leriche, R Fontaine, and S M Dupertuis³ are convinced from a follow-up study of 78 cases that arteriectomy has a distinct value in the treatment of localized arterial obliterative disease. It should be the operation of choice in the imajority of patients because of the four per cent mortality involved in lumbar

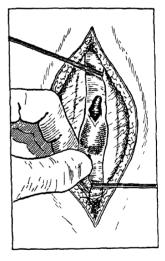


Fig 3—Expressing the clot (Courtesy Proceedings Roy Society Med April, 1937)

sympathectomy Results may be further improved by a combination with subsequent pavaex therapy, heat, massage and exercises The operation is indicated in obstructions due to senile arteriosclerosis, trauma, freezing, after surgical ligature and in favorable cases of embolus and thrombo-anguitis obliterans Arteri-

ography may be used to localize the obstruction. There were no fatalities in this series of 78 cases and relief from symptoms from one to ten years' duration in 43 6 per cent. The percentage of satisfactory results is not as high as after lumbar sympathectomy, but the risk of the operation is much less. If a

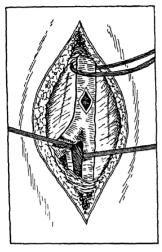


Fig 4—Flushing through from above The lower slings tight (Courtesy Proceedings Rov Society Med April, 1937)

case of embolism is seen early, these authors believe that arteriectomy combined with ganglionectomy may save the limb when embolectomy has failed. The best results in traumatic cases were in resection of a fibrosed arterial cord, with relief from pain, cyanosis and edema

N Akesson⁴ believes that the circulatory disturbances in arterial embolism are partly due to spasm which also favors secondary thrombosis *Eupaverin* may be injected intravenously within the first three hours (1 to 2 ampules containing 3 cg each) and repeated every two to three hours until the circulation is relieved, which may take from one to four days. If there is no result from two injections after a period of two hours, Denk proceeds to operation. As it is impossible to know certainly whether

secondary thrombosis has been prevented or not, Akesson feels that eupaverin should be combined with surgical intervention

After a careful consideration of the anatomic and physiologic basis of arterial embolism, and the results obtainable by embolectomy, arteriectomy, arterial sympathectomy and lumbar sympathectomy as well as venous ligature, passive vascular exercise and drug therapy, P. Funck-Brentano⁵ concludes that the indications for these procedures in cases of arterial occlusion may be listed as follows. If the patient is seen before ten hours have elapsed since onset, embolectomy should be tried under a local

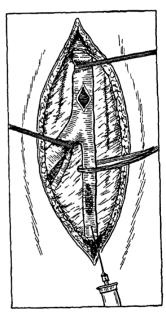


Fig 5—Testing the collateral circulation by slackening the distal controls (Courtesy Proceedings Roy Society Med April, 1937)

anesthetic following careful localization of the obstruction by radiography Strict asepsis must be observed and anticoagulants administered. After the tenth hour arteriectomy is the procedure of choice associated with the same vasodilating and spasmolytic remedies. In both types of operation it is imperative to

support the deficient peripheral circulation by increasing systolic energy (ouabain or digitalis) and stimulating the general arterial pressure (coramine, soluble camphor, pressyl) In cases seen very late arteriectomy is to be preferred for treatment of chronic arterial obstruction

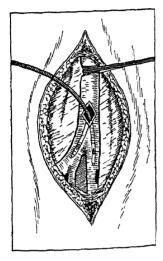


Fig 6—Removal of adherent clot by suction (Courtesy Proceedings Rov Society Med April, 1937)

H W Passler⁶ urges sympathectomy as a final measure after all known conservative measures have failed enumerates the various tests which will enable the surgeon to decide whether success may be expected from sympathectomy After the patient has had his hands and feet immersed in cold water for 20 minutes, he is placed in bed in a cool 100m and given large quantities of tea, aspirin and vasodilating drugs The body is then heated with an arc light and the temperature of the hands and teet recorded continuously. In normal persons the temperature soon regams normal In Raynaud's disease there is an initial delay followed by a very rapid rise in temperature. This reaction is not quite so marked in acrocyanosis In endarteritis obliterans and arteriosclerosis there is a less

marked, more gradual rise in temperature owing to mobilization of collaterals and by direct conduction of heat through the tissues owing to organic obstruction of the vessels. If in spite of these procedures there is no rise in temperature of the extremities, a novocain block of the stellate ganglion as advocated by Leriche is done. If there is no rise in temperature after this intervention, no good is to be expected from sympathectomy

Gask and Rose have shown that after high lumbar anesthesia by means of which the roots of the sympatchtic are excluded from D5 down there occurs in normal subjects a marked rise in the temperature of the feet which is noted also in spastic constriction of the vessels but not in organic obstruction. How-

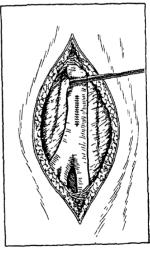


Fig 7—The line of suture completed, the lower controls are removed first (Courtesy Proceedings Rov Society Med April, 1937)

ever, spinal anesthesia as high up as this is fraught with grave dangers, and for this reason it is preferable to use Kirchner's method of spinal anesthesia as advocated by Philippides. One can obtain a paralysis of the vasoconstrictors similar to that which may be expected by later sympathectomy with very small

injections of percaine The results are measured with an electric skin thermometer If indicated the operation can then be performed in the anesthesia present.

S Perlow⁷ stipulates that whereas arterial spasticity is controlled by the autonomic nervous system and can be relieved by sympathetic ganglionectomy, arteriolar spasticity is controlled by a local nervous mechanism or chemical factors, the exact nature of which is not known. It is only in part influenced by the autonomic nervous system and cannot be directly relieved by sympathetic ganglionectomy. The author suggests a method for differentiating between arterial and arteriolar spasticity in the selection of cases for sympathetic ganglionectomy as follows.

The temperature of a histamine flare of the extremities is recorded after anesthetization of the ulnar, posterior tibial nerve and common peroneal nerve respectively. The normal temperatures on the dorsum of the fifth finger and first toe and the normal temperature response to anesthetization are given

A flare of temperature within the normal limits in a skin area, the resting temperature of which is normal, is indicative of a moderate or normal local arteriolar spasticity. If the resting skin temperature is below normal, and the final temperature is equal to or above the normal, marked arteriolar spasm is present.

A rise in skin temperature following nerve anesthetization which is within normal limits in a skin the resting temperature of which is normal is indicative of moderate or normal arterial spasm. If the resting skin temperature is below normal, and the final temperature is equal to or greater than normal, a marked arterial spasm is present. A temperature rise below the normal in

the absence of local vasospasm indicates a very slight arterial spasm.

P. Valdoni⁸ reports the tenth case of embolism of the pulmonary artery cured by embolectomy to appear in the literature An embolus of 10 cm. was milked out and 1 of 27 cm drawn out with a forceps Both respiration and heart activity ceased After artificial respiration, an embolus likewise 27 cm in length was removed from the right branch of the artery Lateral clamps were applied to the pulmonary artery and a continuous suture closed it After closure of the wound blood and air were aspirated through a Pezzar introduced into the eighth intercostal space During the further course still another pleural effusion had to be removed. The author used the technic described by Meyer The circulation can be interrupted for only 60 seconds. In cases in which operation appears impossible eupaverin Eupaverin 18 should be injected also recommended for postoperative treatment

Traumatic Surgery of the Blood Vessels

W Kretzschmann⁹ reports 72 cases of injury of the larger blood vessels from the Payr Clinic, with a mortality of 22 per cent following surgical treatment The mortality from ligation was 114 per cent and from suture 21 per cent He emphasizes the fact that the mortality for suture is five times as great during peace times as in the war period Also the percentage of patients requiring amputation in peace time is almost double that noted during the war period Injury of one artery of the leg never leads to gangrene but if two are injured an attempt at suture should be made in at least one Death is frequently due to the severity of associated injuries Conservative treatment was used in eight

cases with seven deaths. Amputation for gangrene was required in one case Ligation was used in 44 cases with five deaths Here, too, amputation was required in one case Suture was done in 19 cases with four deaths and amputation required in five cases

N. Mankin¹⁰ reports a case in which a segment of the V saphena magna 7 to 8 cm in length was used to repair a defect in the femoral artery due to aneurismectomy with splendid results Carrel's technic was used

Thrombectomy

Operative removal of thrombi from the veins has almost never been carried out. In 1937, Kuhlenkampf fully removed a thrombus from the saphenous vein in three cases as a prophylactic for pulmonary embolism. Before thrombectomy is attempted one must be sure that a thrombus is present and best results will, of course, be obtained in cases in which it is possible to remove the entire thrombus. By removing secondary thrombosis a recurrent embolism may be prevented. The operation is very easy and well tolerated by very ill patients 11

H Frund¹² was able to prevent pulmonary embolism in two cases by thrombectomy of the femoral vein

Varicose Veins

In the injection treatment of varicose veins sodium chloride solution is given preference to morrhuate and quinine hydrochloride and urethane because there is no idiosyncrasy to sodium chloride, such as has been repeatedly observed following the use of the other drugs and it likewise causes less local reaction ^{18, 14}

The only disadvantage of sodium chloride is that it may cause cramps following injection. Even though the technic of injection be perfect, post-obliterative or delayed slough may de-

velop, especially following the use of morrhuate or quinine solutions. Such delayed sloughs are not to be confused with the sloughing due to perivenous inection of the solution The latter can be prevented by counter-injection of distilled water or 05 per cent novocain but this has no effect on the delayed type Schmier has never seen this complication if sodium chloride solution of 15 per cent was used in small doses Recurrence of varices is not so common as reported The development of varices in veins invisible at the time of examination should not be interpreted as recurrence Real recurrence may be avoided by obliteration of the main trunk of the internal saphenous in the thigh Patients should return for inspection every six months for some time after treatment

In cases of recurrence due to recanalization as a result of incompetence of the valves of the saphenous vein and pressure of the resulting blood column, S Z Hawkes and I P Borsher¹⁵ recommend ambulatory saphenous ligation and report a series of 100 consecutive cases They describe the technic in detail They have found the method successful in old as well as younger patients and report healing of chronic ulcers of years' duration within three to five weeks after ligation Bilateral saphenous ambulatory ligation was also done with satisfactory results The site of ligation is determined by tracing the impulse in the saphenous vein It is necessary to ligate close to the fossa ovalis and above the site of the circumflex branches to prevent recurrence in one of the latter The skin sutures are left in situ for two weeks and the varicose veins are not injected for two weeks following ligation because one may thus obtain better cosmetic results, smaller thromboses and less injections Hawkes and Borsher use morrhuate solutions for the smaller veins and sodium chloride-dextrose solution for the Extravenous injection larger veins of the sodium chloride-dextrose solution will cause pain and necrosis Ligation of the saphenous vein before an ulcer is clean may result in cellulitis or thrombophlebitis in the thigh.

V Mazal¹⁶ emphasizes the fact that whereas a certain measure of success cannot be denied to the injection treatment of varices, the method cannot always be used and is therefore deficient It is indicated only in isolated varicose nodules In the larger veins and nodules this treatment will produce a painful hard swelling that annoys the patient long after treatment is over Hypertonic solutions have been known to produce necrosis, pulmonary embolism and Moreover it is frequently necessary to repeat the injection for recurrence Such prolonged and repeated treatment becomes expensive to the individual as well as to the institutions For this reason the author uses the injection treatment only for very small varices or isolated nodules employing In most cases surgical Varicosmon therapy is combined with the injection treatment After ligation of the saphenous magnus, 66 per cent sterile glucose solution is injected into its peripheral end, in quantities varying from 40 to 100 cc for each extremity, according to the number and size of the varices This injection is followed by a pressure sensation increasing to pain. As soon as this pain has reached the lower calf and there is difficulty in injecting more solution the peripheral part of the saphenous magnus is ligated and a section of the vein from 3 to 5 cm is resected The wound is sutured in the usual manner, and the operation repeated on the other extremity designated subcutaneous veins are dissected under ethyl chloride with the Klapp saphenotome The venous blood is pressed out. A compression bandage is then applied for five days. The glucose solution produces an obliteration of the veins and the hard infiltration following other injections is avoided. The patient 18 discharged in eight to nine days. Slight swelling at the ankle will respond to warm baths After three weeks the patient can walk without any difficulty and the cosmetic result is splendid, the tiny incisions leaving only tiny scars which disappear altogether in time.

Results-Five hundred and sixty-six cases were treated, only 152 being limited to one extremity. In one case a suppuration at the site of incision occurred with subsequent thrombophlebitis and septic temperature which responded to treatment This patient had thrombophlebitis before operation, as was discovered later Any injury to the sensory nerves is soon healed by regeneration Recurrence took place in four per cent Of course, a prerequisite for success is that the treatment should be applied early before extensive ulceration has occurred This treatment gives a much smaller percentage of recurrence, affords a radical removal of the varicose veins and gives splendid cosmetic results

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ADRENAL SURGERY

By Gilson Colby Engel, M D

Virilism

From a study of 23 cases of *vurilism* seen during the past eight years, L R Broster¹ concludes that the adrenogenital syndrome is associated with retrogression of the primary and secondary feminine sex characteristics and functions, which may appear as *adrenal pseudohermaphroditism*, *adrenal wirilism*, the *Achard-Thiers syndrome*, which is probably alhed to *Cushing's syndrome*, or *postmenopausal virilism*

Pathogenesis — According to E B Potter² the syndrome of husutism, vuilism and obesity in women is most frequently caused by carcinoma of the adrenal gland, which occurs more frequently in females than in males Hirsutisin and obesity may also be symptoms of tumors of the ovary or pituitary so that a careful differential diagnosis is A surgical removal of the adrenal tumor usually results in disappearance of symptoms and return to normal. In some cases the syndrome may be due merely to a hyperplasia or hypertrophy of the adrenals and in that case improvement may be obtained by removal of one adrenal or of a portion of both In some cases such an operation proves fatal because the remaining gland is unable to supply the hormone of the cortex of the gland in sufficient quantity Administration of cortin may be of aid in these cases

Diagnosis—In differential diagnosis one has to consider arrhenoblastoma,

tumor of the hypothalmus and Cushing's disease Laboratory investigations have given chiefly negative results cases there is some change in sugar tolerance, with a normal elevation from the fasting stage but a slower return to normal A tendency to insulin resistance has been noted Roentgenography of the skull will invariably reveal a small pituitary fossa After injection of iopax a tumor of the adrenal may be revealed either by distortion or relative displacement of the renal pelvis on one side However, the only reliable method of diagnosis appears to be by direct palpation after exploratory laparotomy, when the size of the glands can be determined and a search made for accessory glands and other pathology

Treatment—The author prefers the transthoracic route for surgical approach and uses gas and oxygen anesthesia This is the easiest approach because the vascular pedicle of the adrenal gland permits a slight upward movement and the movements of the diaphragm can be more easily controlled It has the disadvantage of creating an artificial pneumothorax To overcome this an attempt will be made to evolve a subdiaphragmatic route by fracturing the last rib and retracting this upward with the diaphragm Even though more difficult and requiring an expert anesthetist to control the diaphragmatic movements, this method constitutes a step in advance and the patients may be discharged in a fortnight No untoward results followed unilateral adrenalectomy in these cases but after operation there was a definite tendency to restoration of menstrual function, which could be increased by administration of estrogen. Also the abnormal hair began to come out in hunches within 24 hours after operation and although it came in again it was thinner and less abundant cases the hair also showed some change The author emphasizes the in color fact that probably both adrenals are involved in the disease and that one could hardly expect a complete cure to follow ablation of only one gland adrenal seems to be more frequently and markedly involved than the right The operation yielded encouraging results in postpubertal ririlism but not ın prepubertal

Tumors of Adrenal

Most benign tumors of the adrenal cortex produce no symptoms and are usually discovered at autopsy. Only three of 66 cases produced hypertension, precocity and a mass respectively. The changes produced by malignant tumors are not in proportion to the size of the tumor as very small tumors may produce severe symptoms.

Diagnosis—H S Jeck³ states that usual urologic diagnostic methods are generally madequate for the diagnosis of adrenal tumor, which can be better demonstrated by roentgenography following injection of air about the adrenals. In one of his cases a suspected metastatic adenocarcinoma of the adrenal gland was confirmed by exploiatory operation. In the other case a very rare tumor, angioblastoma of the medulla, was diagnosed only at autopsy

F D W Lukens, H L Flippin and F M Thigpen⁴ report a case of adenoma of the adrenal cortex with absence

of the other adrenal gland. This patient displayed almost every feature of Cushing's syndrome. There was no pituitary tumor but the basophile cells showed the hyaline change of Crooke. The cause of death could not be clearly stated in this case. There was no evidence of infection or hemorrhage. There may have been an acute adrenal insufficiency. The patient died on the eighth day following an exploratory laparotomy.

Treatment — Among the surgical routes of approach may be mentioned the transpleural, the lumbar and the transperitoneal, the two latter having the advantage, especially the transperitoneal route as it permits exploration of the glands and of the pelvic organs as well

Pheochromocytoma

This tumor is a neoplasm of the chromaffin cells of the adrenal medulla It occurs primarily in adults but has been seen also in children, and shows an approximately equal sex incidence The symptoms consist in attacks of hypertension associated with palpitation, precordial sensations, epigastric discomfort, nausea, vonuting, pallor and coldness of the extremities, glycosuria, cephalagia and anxiety. The patient seems quite normal between the attacks, which last from 30 seconds to two or three hours Later on the hypertension may become chronic with its usual sequelae Among conditions which have to be differentiated may be mentioned essential hypertension, cardiac neurosis, hyperthyroidism, diabetes mellitus and renal \ H Wells and P G Boman⁵ in attempting to remove these tumors use the Coller Field and Durant anterior approach A three-inch midline incision is made just above the umbilicus permitting localization of the tumor on one or both sides Then a transverse incision is cut from the medial incision to the

peritoneal gutter on the proper side, making possible an early clamping of the blood supply of the tumor without much handling, thus avoiding release of epinephrine into the general circulation. Ether anesthesia is recommended, nitrous oxide and spinal anesthesia being contraindicated. As shock is very likely to occur, materials for blood transfusion should be available.

E Beer, F H King and M Prinzmetal⁶ state that two cases of pheochromocytoma outside the adrenal gland in the local sympathetic distribution have been reported. In their own case removal of a large pheochromocytoma of the left adrenal produced complete relief. This case is the first instance of pheochromocytoma with hypertensive crises in which a pressor substance (adrenalin) has been demonstrated in the circulating blood during a crisis. These authors likewise emphasize the value of perirenal insufflation for the preoperative demonstration of the tumor site.

R Q Atchley⁷ believes that considering the important position occupied by the adrenal gland in relation to the autonomic nervous system, its denervation might be expected to be of benefit in malignant hypertension. Malignant hy-

pertension has to be distinguished from essential or benign hypertension. It occurs chiefly in young persons with no previous demonstrable vascular disease. and has a rapidly fatal termination Retinal changes are common and the patients are subject to emotional excitement Anamnesis will often reveal severe nervous shock, fear, grief or financial catastrophes Hyperthyroidism may be coincident Drugs have given little help in this condition The technic of suprarenal denervation may be carried out through a kidney approach incision, avoiding the twelfth, thoracic, iliohypogastric and ilio-inguinal nerves The left side is usually done first because it is anatomically easiest and the right side can be done after six to ten days

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UROLOGY

By Elmer Hess, M D

Introduction — In the recent past there have been several developments in urological practice that have produced results of note The use of avertin in the manipulation of ureteral stones shows definite promise

A new treatment for Hunner's ulcer is worthy of trial Neuromuscular dysfunction of the bladder has been very carefully studied and the results of presacral ganglionectomy have been noted. The treatment of tumors of the urinary bladder has been fairly well standardized.

The most distinct advance has been in the treatment of gonorrhea with sulfanilamide, while other urogenital infections, particularly those caused by the streptococcus, seem to be responding to

this new drug with startling regularity Whether it is to be the cureall that many of its users have claimed remains to be seen. In all probability, its usefulness will be sharply defined and it will, as a result of experiment and clinical usage, find its proper place in our armamentarium against urogenital infections, both specific and nonspecific

The experimental work on subepithelial papillary lesions as a cause of kidney stones has been studied and the reports favorably received Tumors of the kidney have been definitely reclassified and the usefulness of the x-ray in malignant disease of the urinary tract, while not new, has been further developed Today, the treatment of many renal tumors, both before and after operation, has been developed to the point where it is an essential part of the therapy Conservation of renal parenchyma in surgical attacks upon the kidney has been stimulated by the results obtained in partial renal resection

Pediatric urology comes in for a great deal of discussion, with emphasis placed upon proper early diagnosis in infancy and childhood

Transurethral resection of the prostate, about which there has been so much controversy, is now recognized as a distinct advance in the treatment of bladder neck obstruction. Sufficient reports concerning the procedure, the mortality and morbidity are at hand to properly evaluate its position in urological procedure.

The new technic, or modification of the old technic, for ureterointestinal anastomosis undoubtedly has added much to the safety of this difficult and often necessary procedure

Anesthesia

The selection of a suitable anesthesia for all types of urological procedures is

important. Since most of these cases are bad risks every effort should be made to fit, insofar as possible, the anesthesia to the patient.

Ether, gas oxygen, cyclo-propane, local, epidural, spinal, evipal, caudal, and avertin all have definite indications and contraindications. Immediate and remote safety are important factors to consider. The cystoscopic manipulation of stones in the ureter has usually been done either without any anesthesia or by analgesia with drugs, such as morphine and the barbiturates.

Jarman and W W Scott¹ have demonstrated to their complete satisfaction that the removal of passable ureteral stones is simplified under avertin anesthesia Their technic is to attempt, first, the passage of a 5 F catheter by the stone They then try to pass as many other catheters as possible by the stone These are left in place for 48 hours The patient is returned to the Clinic and 1 Gm of avertin crystals is dissolved in 50 cc of warm, sterile, distilled water This two per cent solution is injected, while warm, directly through the indwelling catheter into the renal pelvis The amount injected is determined by the pain produced from the moderate distension of the pelvis. The catheter is plugged and the patient requested to sit upright in order to facilitate the passage of some of the solution down along the ureter This is allowed to remain in contact with the pelvis and ureter approximately 15 minutes Then the catheters are withdrawn at which time they are slowly twisted and more solution injected directly into the lumen of the ureter The patient is then instructed to void in the erect posture In three instances the obstruction due to stone was so marked that it was impossible to pass a catheter by the obstruction Following the rectal administration

of avertin as a basal anesthetic, three catheters were easily passed beyond the obstruction. In a series of 27 consecutive cases treated with multiple catheters and avertin instillations the calculus was recovered in 25 instances. In 13 cases the stone was recovered as soon as the patient voided. There were only two failures in the series

A L Stockwell and C K Smith² are using pantocaine for spinal anesthesia in one per cent solution. While this drug is nine times more toxic than procaine, they believe that this factor is only theoretically disadvantageous and that in skilled hands there will be no untoward reactions. The advantages are the smoothness of induction, perfect anesthesia for two hours, and possibly more, complete absence of blood-pressure depression, absence of disturbing gastrointestinal reactions, smooth recovery, and total absence of neurological sequelae.

BLADDER

Elusive Ulcer

There is no pathological entity that is so difficult to treat with good results as the elusive ulcer of the bladder (the so-called Hunner ulcer). This condition is among the most painful of all bladder lesions and every possible type of therapy has been tried, mostly in vain, even to bladder resection.

offer the following technic which they have tried in a small series of cases with some beneficial results. Gas anesthesia is used. Injections of 2 to 6 cc of absolute alcohol are given through a long flexible needle using the McCarthy panendoscope. 0.2 cc. are introduced at each puncture. The alcohol in these small quantities is introduced through and around the ulcer. After the treat-

ment the patients are usually kept in bed for 24 hours and are then able to get about as they usually do These men are impressed with the prompt relief of their patients but of course do not know how long the period of relief may be nor how often, as yet, the injections will have to be given. They feel that this treatment carefully administered is without danger. If their subsequent results are as good as their preliminary report shows, this may be the proper way to handle these cases. It is at least worth a trial before more radical measures are taken

Neuro-urological Surgery

Neuro-urological surgery has found a definite place in the treatment of certain urological conditions, and the results have demonstrated most satisfactarily the relief that may be obtained in many types of neuro-muscular dysfunction and intractable pain in the urogenital tract Each year there are an added number of cases and the end results must be thoroughly studied so that the results may be properly catalogued Presacral ganglionectomy has been performed for all types of pelvic and bladder pathology in which relief of pain is the only therapeutic indication. Likewise many types of cord bladder have been subjected to this type of surgery with varying results from complete relief to abject failure

J G Cheetham⁴ reports seven cases of bladder trouble in which, after careful study, this operation was considered applicable. The threefold nerve pathway to the bladder is first, the sympathetics which are the filling nerves, being inhibitory to the detrusor and motor to the internal sphincter and trigone, second, the parasympathetics are motor to the detrusor and inhibitory to the internal sphincter, and third, the pudics which

are motor to the external sphincter and sensory to the posterior urethra

The results of the operation, cystoscopically, are diminished tone of the trigone muscle and of the external sphincter. In the more successful cases, the patient is able to void with greater ease, and residual urine is decreased. In the other group, favorable results may be manifest in the relief of the constant aggravating pain to which the patient has been subject.

This subject of the neurogenic bladder 18 likewise ably discussed by R Van Duzen ⁵ Neurogenic disturbances of bladder function cover many different lesions These should be analyzed and classified as to which system causes the dominating alteration of function doing this, one is able then to use the necessary measures to restore the normal balance of muscle function. It is expecting too much, to expect all cases to be benefited by presacral nerve resection or by giving a choline derivative, in fact, either method may increase the pain and discomfort. This operation is never justified unless the original complaint is more disabling than that which resection of the nerve may produce This operation always produces patent ureteral orifices and predisposes to an ascending pyelitis. The increased difficulty in urination may be controlled by urethral dilatation or adrenaline. It is to be hoped that some drug may be found that will make this operation unneces-Until then the operation is indicated in all cases where hyperfunction of the trigone and hypofunction of the detrusor can be demonstrated, or where in gynecological conditions the condition is so disabling that the operation offers some hope of relief, remembering that there are some cases of undiagnosed or uncontrollable vesical pain which may be helped by this procedure

Tumors

Tumors of the urinary bladder are being recognized earlier than ever before. The painless hematuria, which so often is the only subjective symptom, is being investigated immediately, and as a result these tumors are being diagnosed early and the proper treatment is being instituted, with brilliant results Occasionally hemorrhage is not the early symptom, but this is so seldom as to be almost negligible. However, it occurs often enough to impress upon our minds the fact that any urinary dysfunction calls for complete urological survey.

The incidence of anilin bladder tumors in dye workers has caused the duPont Company to study this subject very thoroughly. The carcinogenic agent is thought to be anilin, benzidine and naphthylamine. However, E. E. Evans⁶ in an analysis of 83 cases indicates that tumors occur in those exposed to benzidine, betanaphthylamine, alpha-naphthylamine, and other nitro and amino compounds, while those exposed to anilin do not have tumors. The average number of years exposure is 12. Repeated cystoscopic examinations are necessary in the control of all employees so exposed.

D M Gay⁷ claims that the process begins with endothelial proliferation in focal subepithelial blood vessels. Occlusion of a vessel causes dilatation of afferent capillaries and edema of the surrounding tissue. Ectasia and proliferation of capillaries form a mass of vessels which persist for months or may be followed by proliferation of the basal layer of overlying epithelium with formation of tumor. This is a disease of the entire bladder and these changes may be repeated indefinitely.

Treatment—The study and treatment of these cases has led to the opinion by R S Ferguson⁸ that multiple papil-

lomatosis of the bladder, both occupational and nonoccupational, is due to circulation in the blood of a cancerigenic agent Therefore, Ferguson and V. D Washburn9 believe that the entire bladder must be treated The only agent capable of this is the x-ray, although fulguration is at times necessary. Technic Five or six small fields about the pelvis are used One hundred roentgens are given to each of two fields daily, with the following factors 200 kilovolts, 25 milliamperes, 100 cm target skin distance, with a Thoraeus filter equivalent to 15 mm of copper The exposure time for 100 roentgens to one field with these factors is about 13 minutes. This type of therapy is contraindicated in the presence of urinary obstruction or infection or any appreciable degree of bladder mucosal congestion

While rare, metastasis to the brain must be considered in cerebral conditions that occur during the treatment of infiltrating tumors of the bladder, even though the bladder lesion is responding to the treatment instituted J A C Colston¹⁰ had such an experience as have others

Prognosis — In summarizing their studies in 72 cases of carcinoma of the bladder, J T Farrell, Jr and T R Fetter¹¹ come to the conclusion that the younger the patient the better the prognosis. In 32 cases their patients were inoperable when first seen and irradiation was the only treatment. This relieves symptoms and hematuria. They believe that radical surgery is often indicated with larger irradiation dosage.

Cystometry

M Muschat, Rose and other investigators have shown the diagnostic and prognostic help that may be had from the intelligent use of the cystometer in neurogenic bladder dysfunction A skilled

cystoscopist can often make practical observations with some degree of accuracy, yet to have these observations verified by an instrument of precision is a great help, particularly in the planning of any surgical attack for the relief of those suffering from bladder paralysis

O. S Lowsley and R W Hunt12 describe the simplest machine yet developed for this important work. It is a small cast cylinder, with a closed bottom and a glass face, divided into two compartments, one of which is water-tight and contains the mechanism for recording the pressure in the second compartment on the dividing diaphragm The pressure is registered by the needle on the dial and is measured in millimeters of mercury The second compartment is hollow and has an inlet and an outlet, the inlet spigot being supplied with a valve for controlling the inflow The cystometer is so sealed that the entire instrument can be immersed in sterilizing solution

Technic of Examination-The examination can be made with either a catheter or cystoscope The procedure being the same in either instance. The cystometer is connected from its outlet by a rubber tube to the catheter or cystoscope, and is placed on the lower abdomen The inlet is connected to the tubing from an ordinary irrigating bottle, such as is used in cystoscopy. The fluid then is allowed to fill the bladder After every 25 cc of fluid are injected into the bladder the inlet valve is closed and the intravesical pressure is recorded. The patient is requested to inform the operator when he has the desire to void, and of any pain or other abnormal sensation This cystometer is small, does not depend upon air, is easily sterilized, with about a one per cent error

M Muschat, J Carp, and C W Charny¹³ consider that the normal blad-

der must be understood before it is possible to estimate accurately the abnormal. Briefly, these factors are Normal Bladder First desire to void 150 to 250 cc with a gradually ascending pressure curve and a maximal pressure of 60 to 80 mm Hypertonic Bladder First desire to void under 150 cc, the curve is very acute, and the maximal voluntary pressure is over 80 mm. Hypotonic Bladder First desire to void is over 250 cc, the curve is flat, and the maximal voluntary pressure is under 60 mm

When one considers that a great many tabetics have bladder dysfunction, it is necessary to know, if possible, how many of these patients have potential bladder disability developing as a result of their disease. It is in these cases of neurosyphilis that cystometric studies should be applied early so that the development of the neurogenic bladder may be spotted early and appropriate steps taken to prevent the progress of the bladder dysfunction.

E L Brodie and I A Phifer¹⁴ reviewed 24 cases of neurosyphilis in which cystometry and cystoscopic findings were used for comparison purposes. They draw no definite conclusions but are impressed with the fact that this method will demonstrate neurogenic dysfunction before frank bladder decompensation takes place. Cystometry in asymptomatic neurosyphilis certainly has a useful place as a guide to both treatment and prognosis.

Gonorrhea

The treatment of gonorrhea in both sexes is still the subject of much discussion. Gonorrhea as such should be treated by the venereologist or the urologist. There are, of course, certain cardinal principles that are axiomatic in the treatment of this disease. The very fact that there are so many remedies

suggests that no one has yet solved the problem

The gonococcus invades situations where chemicals, with bactericidal values, of course, cannot reach, that the patient must build up some immunity goes with-Vaccines have had their out saying trial, bacteriophages and filtrates have all been used and have been found want-P S Pelouze¹⁵ states that the doctor is primarily dealing with a disease, the manifestations of which are due to a highly irritating toxin; that drainage is perhaps the most important factor in the cure of the disease. Pelouze¹⁶ has many suggestions to make for the management and the treatment of those suffering from this disease.

- 1 A uniform history blank should be used throughout the country. There could be no better time to foster uniformity than the present, and the advantages of it are outstanding With such uniformity it would be a rather simple matter to decide on the comparative values of the different types of treatment now in use Also, the study of such histories would do much to teach those using them far more about the disease and the things that are or are not good for it, a gain that would reflect itself in many good ways
- 2 The one in charge of a treatment center should be really interested in the disease Lack of such interest makes for poor work and for poor personnel cooperation. It does little toward disease reduction
- 3 Younger men in such dispensaries should be compensated for the services rendered. In dispensaries of size, this probably should fall on the hospital but, if proper thought were given to possibilities for just revenue from the dispensary itself, this rarely need be a matter of direct cost to the hospital. Hospitals that have been in the habit of charging

small fees for patients able to pay them merely would have to apply the receipts from this one dispensary to the dispensary rather than to their general funds. In smaller dispensaries and in rural communities, other means would have to be devised

- 4 There should be a close alliance between the chiefs of dispensaries, their assistants, their local and state boards of health and the United States Public Health Service as a means of making each one who treats the disease feel that he is a part of a campaign of disease reduction and that some one cares
- 5 So far as such a thing is possible, efforts should be made to carry out an educational campaign among those who treat the disease. In this way interest will be stimulated and better work will result. Also, there would be built up a degree of sanity regarding the disease and its treatment that would reduce to a minium the dangers of the exploitation of treatment methods that have little or nothing to offer. Such things retard advancement and often work to the harm of thousands of patients.

However, in spite of all of the experimental work and the many failures in the establishment of a definite routine treatment, scientific men have continued to experiment with various drugs and combination of drugs both locally, internally, and intradermally During the last year clinical experience with sulfanilamide has focused the attention of the entire profession upon this drug and its curative effects It has been the Editor's experience that in the early acute anterior urethritis, large doses of sulfanilamide given by mouth, where the patient could be kept under constant observation, preferably under hospital conditions, has seemed to act in a miraculous fashion Quite a number of cases were, during the first week of the acute discharge,

immediately relieved of all of their symptoms. The discharge and the gonococcus disappeared from all the urethral secretions and in following many of these cases later, there has apparently been no recurrence of the infection. In some of the chronic cases the results have not been quite so good as, for example, in the chronic gonococcic prostatitis or seminal vesiculitis. The drug acts beneficially even in these cases when associated with the local forms of treatment, such as the urethra overdilatation of sounds, prostatic and vesicle massage and bladder instillations However, in these chronic and subacute cases there has been recurrence of the gonococci in the secretions following the discontinuance of the drug In a very limited number of cases we have been satisfied that the drug is perhaps one of the most outstanding weapons in our armamentarium at the present time

Warning as to its dangers is essential, particularly in the uncontrolled ambulatory patient There are many things to be watched Close observation may spot photo-sensitization of the skin and dermatitis There is some possibility that granulocytopenia and sulfhemoglobinemia may be distinct complications. Often there are symptoms of malaise and marked dizziness. The drug should not be used with other drugs. There is some evidence to support the theory that various toxic effects may be very severe if used in drug combinations Immediate withdrawal of the drug with forced fluid consumption usually is all that is necessary

R D Herrold¹⁷ has treated 30 gonorrheal patients with sulfanilamide. In the first division of 12 patients with chronic gonorrhea of from one to four months' duration, he claims ten cures in between 7 and 21 days. One patient still had positive gonococci after 30 days. These pa-

tients all immediately became virtually symptomless and simulated the carrier state of the infection It must be admitted that some of the cases might have been cured without the use of the drug The average daily dose in this particular division was 20 to 40 grains (129 to 258 Gm) a day and the duration of treatment from one to three weeks The next division was four subacute infections, with one patient cured in 14 days, and in the other three pus and gonococci could be obtained during the 30 days of observation and treatment The dosage here varied from 30 to 45 grains (193 to 29 Gm) a day Very disappointing results, however, were noted in 14 patients with well developed, acute infections, none of whom had ever had gonorrhea before Cures have occurred so far in only four patients. The number of days to cure were 10, 14, 35 and 42 Nine of these patients had anterior infections at the beginning of treatment, three of whom developed posterior urethritis during treatment The shortest period of treatment and observation was ten days and the longest 50 days, while the average period was 29 days Four hospital patients were given 80 grains (513 (mm) of sulfanilamide daily for a period of four days with but slight added improvement. In four patients with associated epididymitis, the swelling and pain disappeared very rapidly, with distinctly less remaining scar of the epididymitis than from other methods of treatment. It is probable that acute salpingitis might respond in a favorable manner Herrold believes that the excretion of the antiseptic is probably greater in the prostate than in the submucous tissues of the anterior urethra He also has noted wide variation in the toleration of individual patients to sulfanilamide He is firmly convinced that sulfanılamıde has comparatively little ir-

ritating effect on the tissues of the urinary tract, that it probably is never excreted in a dilution much greater than 1 1000 In a few cases there has been a trace of albumin before treatment but there has not been an increase during treatment It has little irritating effect upon the kidney. He warns that in the presence of renal insufficiency, the drug should not be given The most common reactions are extreme malaise, sleepiness, headaches, nausea, diarrhea, and general acute intestinal disturbance Cyanosis occurs more frequently with the larger dosage and has seldom been noted when 30 to 40 grains (192 to 256 Gm.) are given He believes that the response is better in the chronic and mild gonococcic infections than in the well developed, acute ones He thinks it is a very valuable aid in postgonorrheal prostatitis and certain infections of the bladder

J E Dees and J A C Colston, 18 who have had a large experience with the use of the drug as prontosil and prontylin, have treated 47 cases of various types of gonococcic infection of the genitourinary tract In 36 of these cases the gonoccocci and urethral discharge disappeared in less than five days. In five cases the subjective symptoms disappeared completely, there was a marked diminution in the amount of the urethral discharge but the gonococci were still present In three cases there was prompt response to the drug but on discontinuance of the drug, there was immediate In two of these cases the recurrence infection disappeared following a second course They feel that the most striking part of their experience has been that in 47 cases there has been no instance of progression of the infection even in those cases which showed no response to the They realize that this, of treatment course, is not a final observation as suffi-

cient time has not elapsed to follow up these cases with definite conclusions They consider the use of the drug as in the purely experimental stage at the present time All workers using the drug emphatically warn against the possibility of reaction and upon the occurrence of these reactions, the drug should, of course, be discontinued The rationale of treatment advised is 75 grains (48 Gm) of sulfamlamide daily for two days, 48 grains (316 Gm) daily for three days, and then 37 grains (24 Gm) daily for from four to eight days No other treatment, either local or general was used Fluids were not forced, alcohol and sexual activity were prohibited The patients were seen every two or three days during treatment Careful examination of the urine for pus and organisms was made on each visit Cultures and smears from the fossa navicularis were done whenever indicated

It seems reasonable to believe that while sulfamilamide will not prove to be a cure-all and the perfect treatment as was first thought, further study and clinical experimentation no doubt will put sulfamilamide in its proper place in the treatment of not only diseases of the genitourinary tract but other parts of the body, that a rationale of treatment eventually will be developed, and that another useful drug will be added to our armamentarium for the treatment of this universal disease

While this drug has been holding the attention of the medical men of the country, other workers have not given up their artificial fever therapy in the treatment of gonorrhea, particularly in the male E H Parsons, P N Bowman and D E Plummer¹⁹ have been able to study 87 young men between the ages of 18 and 49 under rather perfect conditions, i e, soldiers in an Army Hospital These men were all placed in isolation

and were all under constant observation during the period of the study. All the patients were volunteers and co-operated well throughout the period of observation and follow-up. The equipment to produce the artificial fever therapy was two Kettering hypertherms. Patients were classified according to

- 1 Acute gonorrhea Urethritis of less than 90 days' duration
- 2 Acute prostatitis and complications, all of less than 90 days' duration
- 3 Chronic prostatitis and complica-

Persons given the fever therapy were treated for five hours at temperatures of 106.6° to 107° F (41.4° to 41.6° C) every third day. Treatment was continued in each case until at least one treatment was given after the patient was clinically and bacteriologically well

Results—Series 1—Acute gonorrhea 727 per cent were considered cured

Series 2—Acute prostatitis and complications. In this series the fever-treated group did significantly better than the cases in the control-group, while the time required for the treatment of the fever-treated group was approximately one-fourth that necessary in the control-group. An interesting observation was that cases of acute prostatitis with urinary retention and severe pain were uniformly rendered asymptomatic in one treatment.

Series 3—Chronic prostatitis and complications. In the control-group it was noted that less than one-third of the cases could be called cured, whereas in the fever-treated group there were cures in all but two cases. The time required for treatment was approximately four times as long in the control-group as in the fever-treated group. They conclude very definitely that fever therapy accomplishes more cures in gonorrhea in the male than does chemotherapy and that it greatly

reduces the duration of the infection of gonorrhea in the male

J E Potter, F H Redewill and E. G Longley,20 in studying the effects of hyperpyrexia, call attention to the dangerous and even fatal outlook of this type of treatment unless given by skilled operators who understand the management of emergencies They treated 189 cases of gonorrheal infection and complications with 1001 hyperpyrexia treatments with the inductotherm and Kimble cabinet Their most striking results were obtained in gonorrheal arthritis, although all types of gonorrheal infection, with the exception of chronic posterior urethritis, responded most satisfactorily to fever ther-They believe in the addition of active chemotherapy administered intravenously in the form of glucose and mercurochrome, believing that hyperpyrexia is made more efficacious by its combination with chemotherapy

Gonorrhea in the Female-Most of the treatment of gonorrhea in the female falls to the lot of the gynecologist. In the past few years gonococcic endocervicitis and salpingitis usually were managed by the gynecologist and general surgeon, leaving for the urologist the postgonorrheal granular urethritis which is so common in women. In these cases of postgonorrheal granular urethritis excellent results may be obtained by overdilatation of the urethra and the instillation of silver nitrate from one per cent up to the use of the solid stick for swabbing the urethra The diagnosis of gonorrhea is perhaps more difficult in the female than in the male Often it is almost impossible, where the disease is known to exist, to isolate the gonococcus from the vaginal secretions

- J G Marthens²¹ treats the disease in women in the following manner
- 1 The parts are thoroughly cleaned and labia separated They are cleansed also

2 Each patient is catheterized, a number 18 French glass catheter being used. Any pathology present is detected by this sized instrument. A two per cent *silver albuminate solution* is injected into the bladder and urethra, using a special metal tip which will fit any syringe

- 3 A bivalve speculum is inserted and the cervix brought into view. The vaginal canal is douched with one quart of hot potassium permanganate solution, 1 to 8000
- 4 The parts are thoroughly dried The cervical canal is mopped out by cotton on metal probes. The same style probe is used and the canal painted with a 20 per cent mercurochrome solution
- 5 Next the entire vaginal vault and cervix are painted with a two per cent mercurochrome solution.
- 6 If the cervix is edematous and angry looking, ten per cent ichthyol in glycerin is placed on a tampon and inserted into the vagina, up against the cervix. This treatment continues until the cervix approaches its normal appearance when mercurochrome is used on the tampon, 1 to 2000 strength.

The above treatment is given three times a week. The tampon remains in the vagina for 24 hours. On removal, the patient is instructed to take a hot iodine douche, one teaspoonful to two quarts of water. On the days she does not report for treatment or is not carrying a tampon, she is instructed to take two douches daily. She is instructed to be as quiet as possible, drink large amounts of water, keep the bowels open and especially to avoid strenuous exercise.

This treatment is carried on to the menstrual period, when treatment stops. The first day after the menses are over the patient is instructed to report to the office for an examination and treatment. Smears are again taken as in the original examination.

The treatment takes from three to four months In each month the patient will lose from seven to ten days when she is unable to take treatment

After the acute symptoms are over, if Skene's glands are infected they are destroyed by fulguration. If an abscess of Bartholin's gland is present, it is incised and drained. If the condition does not develop into an abscess, and when all active inflammation has subsided, the gland is destroyed by fulguration.

After the urethritis has subsided, gradual *dilatation* is started Straight sounds are passed, and not oftener than twice a week.

If gonorrhea of the rectum is present, instillations of a mild silver salt are used, and after the acute stage has subsided the rectum is examined and any foci of infection remaining are touched with a silver nitrate solution.

"The treatment as outlined I employ in my private practice as well as in the clinic. The different forms of heat therapy have not been successful in my hands. By the above method of treatment, which is controlled by frequent examination of smears, one can watch his patients more carefully and detect any complications early. Salpingitis, arthritis, and abscess of Bartholin's gland are complications that seldom appear under this method of treatment."

After all smears are negative the patient is instructed to report after each menstrual period for three periods to be re-examined

Before discharging a patient a cystoscopic and urethroscopic examination is made and this is followed by an intracutaneous injection of a foreign protein to see if any hidden foci have been missed

"In the past two months I have been using gonococcus filtrate (Corbus-Ferry)

as a provocative measure. My results will be published at a later date "

Endocarditis — That the gonococcus can occasionally get in the blood stream and attack other organs in the body is undoubtedly true There are many cases on record of gonorrheal endocarditis involving the aortic, mitral, and pulmonary valves This possibility, however, must always be considered when cardiac symptoms complicate any form of infection by the gonococcus N F Ockerblad and H E Carlson²² report a case of tricuspid endocarditis in a male, aged 57, which they believe was due to the liberation of the gonococci into the blood stream as a result of a urethral dilatation emphasize the fact that this disease is not common, that it most often affects the left heart, but occasionally, as in another case which was found in the literature. the tricuspid valve was affected

Examination of the Bulbourethral Glands—A Firestone²³ calls attention to the necessity of an examination of the bulbourethial glands as a routine procedure in all acute and chronic stages of gonorrhea With the bladder preferably full, the prostate and seminal vesicles are first palpated and massaged, and their secretions examined The patient then voids The bladder is filled with a clear antiseptic solution, and with the finger in the rectum and the thumb held in approximation against the permeum, the enlarged gland may be palpated just below and beneath the bulb The right and left glands are alternately palpated and massaged, with pressure being applied downwards and laterally from the bulb The patient then voids into three glasses, the first glass containing the expressed secretions, the second is clear, the third may also contain shreds and some pus The shreds may then be removed with pipette or loop, dried, fixed, properly stained and examined micro-

scopically. With this routine examination, a much larger percentage of pathological glands will be found and they may easily be the cause of a protracted gonorrhea or a persistent morning drop or urinary shreds

Treatment—The treatment of acute Cowperitis consists of gentle massage of the glands, diathermy, incision and drainage in case of abscess, preferably through the perineum Emphasis is placed upon the necessity in all chronic urethral diseases for the elimination of Cowper's glands as a focus of infection

KIDNEY

Anomaly

The anomalous kidney must always be considered in all cases where a tumor is found in the pelvis or abdomen that cannot be readily identified There may be no symptoms referable to the urinary tract and often these ectopic and pelvic kidneys are only found after the abdomen 18 opened It is then often dangerous to remove these renal masses as there may not be other renal parenchyma to carry on urmary function Often these cases are only discovered at autopsy. In all cases where symptoms are referable to the urinary tract nothing less than a complete urological survey will suffice The various problems of treatment will often tax the ingenuity of the most skillful operators

A R Stevens²⁴ reviews a series of 27 pelvic single kidneys. Many of these were removed with fatal results. Most of these cases are among the earlier cases. Today with modern urological methods these errors should never be made. Surgical attack on these kidneys must of necessity be of a conservative nature.

One must likewise be alert for the congenital solitary kidney Again, these

cases should all be diagnosed and treatment for existing pathology should be conservative ²⁵ Often the same general conditions exist in hypoplasia. If one kidney is hypoplastic and its hypertrophied fellow is diseased, treatment of the hypertrophied organ is conservative, while the hypoplastic organ may be the source of the symptoms. In the latter instance the hypoplastic organ may be removed. J. C. Kimbrough²⁶ reports such a case. He emphasizes the fact that we do not understand why these hypoplastic organs give pain. It must be some sympathetic disturbance.

G J Thompson and J. M. Pace,27 in discussing renal ectopia, call attention to the fact that treatment in the majority of these cases is seldom indicated Most of these organs function normally and often give no evidence of their presence Many of these cases must. however, be subjected to surgical attack Where there are two kidneys, the one suffering from gross pathological changes may have to be removed Often a conservative pelviolithotomy may have to be done to remove calculi or for drainage purposes, while most of these kidneys, if infected, may be successfully treated by cystoscopic methods

Calculi

A great many studies have been made during the past year on the cause of renal calculi. It is well known that geographic distribution plays some part in the formation of stones. Certain races are less subject to stones than others. Vegetarians will form uric acid stones. There is a relationship also between the formation of calculi and fractures, osteomyelitis, empyema, hyperparathyroidism, osteitis cystica, and congenital renal conditions. Uninary infection and obstruction play their part. Foci of infection and vitamin. A deficiency may be causes. Wm. J. Ezickson and C. E. Kremer,

Jr, 28 report their study of many microscopic sections from 14 kidneys removed under the diagnosis of nephrolithiasis These sections show evidence of tissue insult, infection, old and new, with scars and cellular infiltrations in cortex and medulla Polymorphonuclear leukocytes are seen forming minute abscesses throughout the parenchyma Occasional cysts are seen in the cortex Inorganic deposits in epithelial and interstitial elements are found in the collecting tubules and atrophy of pelvic epithelium associated with subepithelial fibrosis There is cornification of the pelvic epithelium, vacuolization of epithelial cells combined with a variety of hyalin and granular degenerations of glomeruli and tubules There is occasional amyloid deposit, cellular infiltrations of lymphoid type with occasionally a prominent number of eosinophiles, sclerosis of the arterioles and all forms of necrosis with healing and scar tissue formation

A Randall²⁹ asks the questions From what does the stone take origin? Where does it first arise? How does it grow? Why is it for a time stationary? Why are stones so often found in only one kidney? And why, when certain theoretical morbid states exist, does it fail to occur? He believes and attempts to prove that renal stone originates by a growth in an original subepithelial papillary lesion, and has been able to demonstrate rather progressive steps in the growth of the calculus in this location He offers the thought that these subepithelial calcium plaques eventually lose their covering membrane and from then on are bathed in the urinary excretion and form the nucleus for a further enlargement and formation of the stone The treatment of the disease depends entirely upon the size of the stone, the infection present, and the destruction of the renal parenchyma

G. D. Oppenheimer and H Pollack³⁰ discuss the dietary treatment, and while they do not condemn the treatment completely, are satisfied that the high vitamin acid ash diet has not caused disappearance or reduction in the size of renal calculi of the alkaline earth type In a study of 27 cases they did not see complete or partial solution of the calculus at any time during their study.

Much work has been done on hyperparathyroidism and its relationship to renal calculi. Chute, Albright, Bloomberg, and others, have, after removing stones, discovered tumors of the parathyroid gland and have removed them without apparent further development of stones in these particular cases 31

If the blood calcium is above 11.5 and the blood phosphorus below 3.0, it is perfectly possible that there is a hyperplasia or tumor of the parathyroid. In an endeavor to ascertain the recurrence of stones following operations for nephrolithiasis, F. P. Twinem, 12 in a study of 314 cases operated upon for stone, found 20.9 per cent recuired after pyelotomy and 28.0 per cent after nephrotomy. The percentage of recuirence was greater following operation for multiple stones than for single stones. Heminephrectomy should be employed more frequently than it has been by most operators.

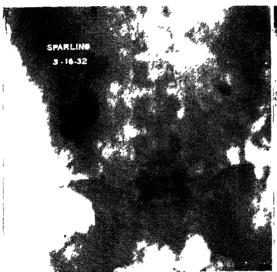
This is a very interesting observation because during the past few years the author ¹³ has been doing a great many renal resections for various pathological conditions located focally in the kidney. A complete résumé of the indications for partial resection of the kidney is listed and the following is said concerning calculous disease.

Hydronephrosis, Pyelonephritis, Pyonephrosis, Calculous Disease—Calculous disease may be unilateral or bilateral, with or without nephrosis, sterile or infected Where the disease is bilateral the

problem that presents itself is often sufficient to tax the magic ingenuity of a Keller or a Thurston There have been five cases of bilateral calculous disease that have required the total sacrifice of one kidney (calculous pyonephrosis complete) and the removal of a large section of the functioning fellow because of multiple calculi, dilated infected lower calyx or localized parenchymal or perinephritic infection

why a lower pole is not left behind with a stone in it or with a dilated infected calyx to become a regular cesspool for future infection and the source of continued renal infection. That is why one tried to level off the pelvis in resection so there can be no stasis

Take another case This x-ray (Fig. 1) is of a patient with a stone in the lower pole of the left kidney and a completely destroyed calculous pyonephrosis



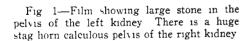




Fig 2—Satisfactory pyelogram with Neo-Iopax showing the left kidney (Courtesy, Western Journal of Surgery, March, 1937)

In discussing the symposium on heminephrectomy at the meeting of the American Urological Association in Boston. Quinby made approximately the following statement. He said that he wondered if many resections were done in the presence of infection, whether it might not later be necessary to nephrectomize because no surgeon had "the microscopic eye" and couldn't tell how much infected kidney substance was being left behind. The answer to that question is this. Most infected kidneys get well if and when urinary stasis is relieved and free drainage down the ureter is obtained. That is

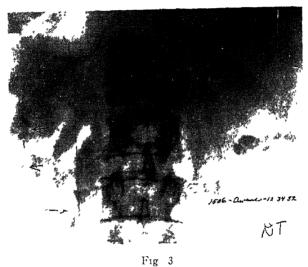
on the right side. The lower calyx in this kidney was filled with pus and débris and this large stone. Partial resection of this lower pole was accomplished without any difficulty. Figure 2 shows the pyelogram after the resection and before total nephrectomy was done on opposite side.

Here is the plate from another interesting case (Fig 3) There is a large stone in the ureter and another large stone in the kidney pelvis. There are many stones in the lower pole of the opposite kidney. This patient required nephrectomy on the right side and a resection was done on the left side with

removal of all the stones in the lower pole of this kidney. The same surgical procedure of resection of the kidney is often necessary in anomalous conditions of the kidney ³⁴

Many of these pathological conditions are likewise thoroughly discussed by A E Goldstein and B S Abeshouse,³⁵ who give as their indications solitary serous or hemorrhagic cysts, hydatid cysts, localized hydronephrosis or pyonephrosis, with or without renal calculi,

losis to be the subject of much controversy between the urologist and the rest of the profession. There is no question that if tubercle bacilli are found in the urine there must be a genitourinary lesion. Due mainly to the work of Medlar and others, this lesion theory has been placed upon a rather firm basis, and yet it is very difficult for many of us to accept the statement that tubercle bacilli cannot be filtered through normal kidneys without having an active lesion,



(Courtes), Western Journal of Surgery, March, 1937)

benign tumors, localized cortical abscesses, renal carbuncles, renal infarct and renal fistula. In extensive bilateral disease they emphasize the fact that resection becomes an operation of necessity in tuberculosis, calculous pyonephrosis, and rupture of the kidney.

The author adds that it is absolutely imperative for localized disease causing symptoms that cannot be controlled by the ureteral catheter, in pelvic and single kidneys or hypertrophic kidneys with hypoplastic fellows

Tuberculosis

A great deal of recent work has caused the proper treatment of renal tubercueven though it may be microscopic. That there are a great number of cases of renal tuberculosis that spontaneously heal is undoubtedly true However, the urologist is usually on safe ground when he advises nephrectomy for the kidney that is constantly sending out showers of tubercle bacilli. Most men are satisfied that an early diagnosis of renal tuberculosis calls for early nephrectomy, but it must be emphasized that the smegma bacillus is commonly found in the voided urine of women, that it is difficult to distinguish the smegina from the tubercle bacıllus by all ordinary methods and that this organism must be ruled out in every

case before a definite diagnosis of urogenital tuberculosis may be made

R M LeComte³⁶ reports two cases of renal tuberculosis that have caused him to restudy the whole situation The first case was a single woman of 36 years in whom left renal tuberculosis had been diagnosed elsewhere five years before. She had had three clinical relapses, each relieved by constitutional treatment, since the diagnosis had been made In June he removed a closed left renal tuberculous pyonephrosis The second occurred in a married man, aged 42 years, who had had epididymal tuberculosis at the age of 14 years Urologic study in September showed cortical abscess with calcifications and tuberculosis of the right kidney Nephrectomy was advised but refused on the advice of his physician

As it stands today, the physician who is charged with the treatment of patients with urogenital tuberculosis is somewhat in doubt as to whether he should submit those with renal tuberculosis to the urologist for study and probable surgery or, since renal tuberculosis may both be bilateral and healed by general measures, whether he should not take a short cut, omit detailed urologic study and particular judgment and treat his patient by general and hygienic measures alone. This stand seems to be based largely on studies of Medlar, Thomas and Harris

Once the lesson, however, has progressed to the extent that the pelvis is involved and pyelographic changes are evident, surgery is the only treatment

If tubercle bacilli and pus are found in the urine from a kidney without functional depression or pyelographic change and contamination can be excluded, a delay for these to develop may be in order but it need not be a long one and, if the pyuria and bacilluria persist, nephrectomy may be done without great fear that the operation will prove to be

an unnecessary one On the other hand, while it is possible that healing may go on to a complete cure without nephrectomy in such a case, it will be a remote and extremely rare result

If pyelographic evidence of tuberculosis is found in addition to pus and bacilli in the kidney urine, only partial healing and regression, never cure, can be expected. The patient and surgeon must then choose whether to take the chance of cure by nephrectomy or to spend an indefinite time in a sanitarium, on trial, so to speak, only to face nephrectomy as a probability in the long run

If the kidney that is to be left is functionally sufficient, secretes urine free from pus and bacilli and is normal anatomically on pyelogram, it may, for practical purposes, be considered as being free from tuberculosis. If it should happen to be the seat of a silent preclinical lesion of tuberculosis, and accordingly not susceptible to diagnosis by our present means, no matter how many examinations are made, the last may be as much in error as the first. If the findings are at all questionable, however, a sufficient number of examinations to establish accuracy should be done.

It is recognized, of course, that an accurate diagnosis of renal tuberculosis can be made in many ways other than those outlined above and that *nephrectomy* is only the one step in the treatment *Sanitarium treatment*, or at least home treatment under the care of a sensible phthisiologist, should supplement the effort of the urologist

J A Lazarus³⁷ states that postoperative wound disruption is a frequent complication following nephrectomy. He employs a combination of *ultraviolet* radiation and suberythema doses of roentgen therapy immediately following operation. He advocates roentgen therapy to cases of ulcerative tuberculosis

of the bladder as an excellent means of controlling the pain associated with this complication, and believes that this type of therapy should begin immediately after operation and has distinct advantages in controlling and preventing postoperative tuberculous fistulas It would seem that if the operation had been cleanly done and the stump of the tuberculous ureter properly handled that these postoperative fistulas would be very rare It is doubtful if they ever occur when there has been a complete removal of the tuberculous kidney, its lymphatics and the glands of the hilus unless a foreign body of some type has been left behind In the Editor's experience, in a series of over 200 cases of tuberculosis of the kidney removed by nephrectomy, postoperative sinus formation occurred in only two cases, one where a piece of catgut acted as a foreign body, the other where a gauze wipe had been left in the wound In both cases the fistulas healed promptly with the removal of the foreign body

Tumors

In the diagnosis of kidney tumors, G G Reinle and L Kindall³⁸ give a simple anatomical classification of renal tumors

- 1 Of excretory portion
 - I Fetal tumor—polycystic kidney
 - 2 Adult tumors
 - (a) Benign papilloma
 - (b) Carcinoma
 - (1) Papillary
 - (2) Epidermoid
- 2 Of secretory portion
 - 1 Fetal—adenomyosarcoma Wilms tumor
 - 2 Adult tumors
 - (a) Papilloma (intracystic)
 - (b) Adenoma.
 - (c) Carcinoma
- 3 Extra renal origin—sympathetic nervous system
 - 1 Neuroblastoma
 - 2 Paraganglioma

An embryological classification of renal tumors follows

- I Derivatives of Wolffian duct (pelvis, calyces, collecting tubules).
 - 1 Benign
 - (a) Polycystic kidney embryonal
 - (b) Papilloma of pelvis
 - (c) Cystadenoma
 - 2 Malignant
 - (a) Papillary carcinoma of pelvis.
 - (b) Epidermoid carcinoma of pelvis
 - (c) Adenocarcinoma Secondary to cystadenoma
- 2 Derivatives of nephrogenic tissue (glomerulus, convoluted tubules, and loops of Henle)
 - 1 Benign cortical adenoma
 - 2 Malignant
 - (a) Carcinoma
 - (1) Clear cell papillary
 - (2) Granular cell papillary
 - (3) Alveolar adenocarcinoma
 - (b) Mixed tumors
 - (1) Wilms adenomyosarcoma—embryonal
 - (2) True teratoma
- 3 Derivatives of extrarenal tissue (sex cells, lymphoid tissue, sympathetic nervous system)
 - 1 Epiblastic
 - (a) Sex cell carcinoma
 - (b) Neuroblastoma
 - (c) Sympathoblastoma
 - 2 Mesoblastic
 - (a) Lymphosarcoma
 - (b) Neurofibroma
 - (c) Neurogenicsarcoma

There is no question that the only treatment of tumors of the kidney is *surgical*, however, they must be viewed for the purposes of treatment under two heads, namely, tumors of the parenchyma and tumors of the pelvis. Ninety-five per cent of the former are more or less radiosensitive and a preoperative course of *radiation* should be given. Emphasis must be placed on the fact, however, that radiation never cures and surgery should

always follow. On the other hand, tumors of the renal pelvis are radioresistant and should be treated surgically at once, removing the ureter when indicated and a portion of the bladder wall **Postoperative radiation** is advised against metastases or local recurrence ³⁹

The technic of this therapy is 200 k v with the Coutard technic, filtration with 05 mm of copper and the total tumor dose ranging from 1600 to 3500 r, employing from two to four portals of entry A D Munger⁴⁰ is treating his cases with these factors and others with 650 k v constant potential, filtration 11/4 mm of lead, the equivalent of 10 mm of copper, in addition to the fixed filter in the tube itself which is \frac{1}{8}-inch steel, 1/4-inch aluminum, 4 mm bakelite and 3/4-inch water, multiple ports with 300 r per area per day, distance 72 cm Each area receiving its quota in rotation until the completion of the series which consists of 2100 to 3000 r per skin area While to some who are not familiar with supervoltage therapy, this statement will sound heretical, nevertheless the very interesting clinical course of these patients to be detailed in a later communication, so far at least, amply justifies the procedure

It would only be natural to assume that under such enormous dosage, the pathological picture detailed in Hartman's experimental studies would find its clinical parallel here. On the other hand, this parallel does not obtain There is not infrequently, during the course of treatment, some albuminuria and occasionally some casts with evidence of func-Regression under tional disturbance cessation of treatment has rapidly taken place and a permanent nephritis has not developed, or, in certain instances, a marked delayed nephritis has ensued In each instance, this has regressed to the physiological state, indigenous to that

kidney before irradiation. In two instances, irradiation was instituted postoperatively only. In all other cases, irradiation was instituted for maximum reduction in the size of the tumor.

LYMPHOGRANULOMA INGUINALE

Granuloma inguinale is a venereal disease characterized usually by raised. sharply defined, beefy red, convoluted lesions on the skin of the genitalia and surrounding parts The lymph glands are not involved and it spreads by con-It runs a chronic course, causing much destruction, scar tissue and con-Lymphogranuloma inguinale, tractions on the other hand, starts with a primary lesion of the genitalia with secondary involvement of the lymph nodes, which eventually break down and suppurate from multiple foci In the female the lesions are mostly perirectal because the draining lymph nodes are in that location Eventually scar formation and contractions of the rectum take place There may be secondary elephantiasis and fistula formation of the vulva and rectal tissues with this stenosisesthiomene 41 The diagnosis of granuloma inguinale is made from clinical appearances and by finding in smears from the diseased tissue of certain large endothelial cells with intracellular and extracellular inclusion bodies The diagnosis of lymphogranuloma inguinale is generally possible from the clinical picture and course, with lymph nodes finally suppurating from It is confirmed by the multiple foci specific intradermal Frei test, made with an emulsion of sterilized pus from the lymph node (unopened but about to suppurate) of a known case of lymphogranuloma inguinale The therapy of both diseases is still problematical Surgery may be employed in certain in-

stances Although some cases respond at times to *intravenous injections* of antimony salts, yet there is much to be desired in the treatment

C L Wilmoth⁴² states that the results with Frei antigen in the treatment of lymphogranuloma inguinale has not been very successful and for that reason the infected glands are excised During the past three years 42 patients have been operated upon In each case operation was performed before the skin over the infected glands had become involved. In many instances, had operation been postponed until the Frei test was positive, the skin over the infected glands would have become adherent and possibly somewhat reddened In such cases healing by primary intention is infrequent Contrary to general belief, elephantiasis does not follow excision of the superficial subinguinal group of glands There is much less obstruction to the flow of lymph following a clean dissection of the glands than from a long drawn out inflammatory process which follows conservative measures or the injection of various proposed substances into the inflamed glands

M S Wien and M O Perlstein⁴³ describe three types of ulceration of the skin in this disease

- 1 Ulceration of the skin only
- 2 Ulceration of the skin secondary to a previous lymph gland involvement
- 3 Ulceration developing on an existing esthiomene

C C Tomlinson says that it is difficult for him to accept this cutaneous ulcerative phase independent of an underlying suppurative lymphadenitis

H M Robinson sounds a warning against the positive Frei test. He says that it means past or present lymphogranuloma inguinale, but that not every lesion that gives a positive Frei test is this disease

P A O'Leary has had the opposite He wishes to stress the experience point that there is sufficient evidence to prove that lymphogranuloma inguinale is a systemic disease and not solely a genital infection It seems that the treatment of these conditions is still rather Certainly, certain types of uncertain cases are helped by the intravenous injection of antimony salts, however, results seem to be obtained also from the intradermal injection of Frei antigen, and some of the ulcers are healed by the exhibition of antisyphilitic therapy.

PEDIATRIC UROLOGY

Due to the efforts of Meredith F Campbell, who has written two books on Urology in Children (The Macmillan Company, Publishers) and which are recommended to anybody interested in the subject, there has been added stimulation to the study of the urological tract in infants and children, and the previous fear of pediatricians and general practitioners toward referring these small patients for cystoscopic examination has been very generally allayed It is possible with the instruments now in the armamentarium of the modern urologist to examine cystoscopically almost any child of any age. There is no question that children are disturbed by many urological conditions. As a matter of fact, many adult urological problems would never be seen had the unological problem been discovered in childhood, many cases of hydronephrosis, pyonephrosis, tuberculosis and calculous disease start in childhood and are not discovered until adult life

R L Anderson and J J Lee⁴⁴ discuss all of the various urological conditions that children have They call particular attention to the fact that medical literature abounds with the term "pye-

litis," and most often wrongly so. They say that they seriously doubt that pyelitis per se exists What is actually present in many cases is pyelonephritis chills, pain, vomiting, and pyuria indicate parenchymal involvement of the kidney. Many of the so-called cases of pyelitis respond rapidly to the use of urinary antiseptics and alkalies alone In these there is free drainage into and out of the urmary tract They may be of hematogenous origin if recurrence takes place All cases of persistent pyuria are almost invariably due to some form of obstruction with urinary stasis As an example of what can be accomplished, Campbell reports a series of 249 cases, age four and older, in which the clinicians had diagnosed enuresis The symptoms were mainly frequency, urgency, dysuria, burning on urination, and enuresis Pyuria was present in approximately 25 per cent of the cases Medical treatment, physical therapy, or psychotherapy had failed in all cases Urologic examination revealed that approximately 60 per cent of the children had a definite organic basis for the urinary symptoms cystoscopic findings included practically every known lesion of the urinary tract Stone, tuberculosis, all gradations of cystitis, verumontanitis, upper urinarytract infections, neuromuscular disease of the bladder outlet, involvement of the posterior urethral valves, urethral stricture, and many others

That hydronephrosis in infancy and childhood is common is strikingly brought to attention by H L Kretschmer, 45 who reports a series of cases of this disease. He has this to say concerning the treatment. The cases of obstruction at or in front of the bladder neck call for suitable correction, namely, dilatation of strictures of the urethra, destruction of congenital valves, either by means of fulguration through the urethroscope or

surgery, relief of bladder neck obstruction with a resectoscope or open surgery. Those due to stricture at the vesical end of the ureter require repeated dilatation by means of the cystoscope and ureteral catheter followed by pelvic lavage Occasionally nephrectomy is necessary because of severe infection in the obstructed kidney Strictures at the ureteropelvic junction associated with infection are treated by the indwelling ureteral catheter. dilatation, and pelvic lavage and if this fails, surgery is indicated Conservative surgical procedures are often indicated Included in these are division of aberrant vessels, nephroureterolysis, and the various plastic operations that have been designed for operations upon the renal pelvis Many of these cases, however, will require nephrectomy

Pyelonephritis in children is usually secondary to obstructive lesions which are of the congenital anomaly type, according to F. F. Hatch 46 He further states that pediatricians frequently are not sufficiently alert when they treat chronic pyuria for months without the aid of urologic consultation Authorities generally agree that, if after a few weeks of general medical or pediatric treatment, children are not relieved of symptoms of pyuria, a cystopyelogram is indicated, followed by pelvic lavage, if no obstructive lesions are present. Thorough general study of patients with eradication of focal infections or obstructive lesions is indicated early in the care of persistent cases Congenital ureteral stricture does not exist primarily but results from pyeloureteritis, which is secondary to atonic Early treatment of ureteral dilation pyelitis by catheter drainage should lessen the occurrence of stricture

Hemorrhagic nephritis is quite common in children following acute infectious diseases. There are three major complications. (1) Renal failure, (2) hyper-

tensive encephalopathy or so-called eclamptic uremia, and (3) cardiac failure M I Rubin and M Rapoport⁴⁷ report a series of cases where one or all of these complications have existed in children with hemorrhagic nephritis. In their experience, hypertension has been present in all cases manifesting signs of cardiac insufficiency

The treatment of the acute nephritic with cardiac symptoms resolves itself into two components (1) Measures directed at reduction of the peripheral resistance and load, (2) measures directed at improving the activity of the heart itself

In the attempt to reduce the peripheral resistance against which the heart must work, the following therapy is utilized

- 1 Magnesium sulfate is given intramuscularly in suitable doses to relieve the hypertension. It is also administered orally and rectally
- 2 Fluids are restricted in an effort to maintain the blood volume at a minimal level, thus keeping down the peripheral load. Following the disappearance of the acute cardiac manifestations, fluids are no longer restricted.
- 3 Phlebotomy has been employed, especially in those patients with frank cardiac decompensation. This must be done rapidly, and a moderately large amount of blood must be withdrawn. The resultant anemia has been remedied by small transfusions when the patient has recovered from the heart failure.

In attempting to improve cardiac efficiency, the following measures are employed

- 1 Digitalis. Rapid digitalization over a period of 12 hours is effected by using 45 mg of whole leaf per kilogram of body weight. This has been given hypodermically as fat-free tincture.
- 2 Morphine has been employed in adequate narcotic doses

- 3 The oxygen tent has been used when deemed necessary The undoubted value of oxygen in the anoxemia of acute cardiac decompensation requires no comment
- 4 Small doses of hypertonic glucose (10 to 20 cc of 50 per cent glucose) have been given. It has been shown that the glycogen content of cardiac muscle is decreased during heart failure, and that unless the blood sugar is kept at high levels the glycogen stores of the heart are not replenished.

PROSTATE

Transurethral Resection

During the past year many men who started out enthusiastically to do transurethral resections for hypertrophy of the prostate have given them up and gone back to the old suprapubic or perineal operation. They have come to the conclusion that in their hands the suprapubic operation, principally, is the safest. However, this is not the attitude of many of the men who have made a close study of the scientific possibilities and advantages of the transurethral procedure.

H C Bumpus, Jr,45 in reviewing the development of transurethral surgery states that many gazed upon the interior of the bladder for the first time through their new resectoscope and attempted the removal of what they believed was obstructing prostatic tissue That efforts of this type should prove disastrous was to be expected types of surgery, errors in technic, although regrettable, can easily be remedied An incised artery may be repaired, a perforated bowel sutured, a cut ureter ligated or transplanted, but a single mistake in excising tissue beyond the anatomical boundaries is irreparable

Urinary extravasation or rapidly developing peritonitis, to say nothing of fatal hemorrhage and complete urinary incontinence, are the results of such All these disasters, and many errors others, have occurred many, many times Therefore, the factor which constitutes the greatest limitation of this procedure is not the instrument used, nor the operation, but the training of the operator Truly, as Day originally said, "This is a specialty within a specialty" Records are now available of thousands of cases demonstrating that with proper care and careful technic that, in the hands of transurethral resection trained men. offers the lowest mortality rate of any method for correcting urethral obstruction resulting from prostatic enlargement

G J Thompson⁴⁹ takes exactly the same attitude and in discussing the selection of cases, states that many urological surgeons feel that resection should be reserved for small bars and contractures and for all patients who are poor risks for operation. He feels that following an apprenticeship of several hundred cases, the resectionist can generally perform just as complete a prostatectomy by the transurethral route as can be performed by any other method of operation.

There are still many men who believe as does H C Rolnick and L A Riskind⁵⁰ that transurethral resection should be reserved for those patients who are poor risks and where the prostate is not large

One of the finest contributions to the technic of transurethral prostatectomy has been the contribution of R H Flocks⁵¹ on the arterial distribution within the prostate gland. The distribution of the arteries within the prostate gland has been studied in the infant and the normal adult, the prostate showing

hyperplasia, carcinoma, and those that have been subjected to transurethral re-There have been found two groups of arteries within the prostate, an external capsular group which shows little change with age and with the occurrence of hyperplasia, and an internal group, the urethral group, which enlarges significantly with age and very markedly with hyperplasia The latter is very important in the consideration of transurethral prostatic resection and local repair following this operation for two reasons (1) Anatomical arrangementthe urethral group of arteries penetrates at the prostatic vesical junction and then turns distally in a course more or less parallel to the urethral surface, (2) its ultimate destination This group of arteries forms the main source of blood supply to the hypertrophied portion of the prostate

TESTICLES

Tumors

The diagnosis of swellings of the testicle is very important, principally to the patient. Tumors, both malignant and nonmalignant, must be differentiated from gummas and chronic inflammatory conditions, such as tuberculosis. The vast majority of tumors are malignant and the prognosis even under the best of therapeusis is usually unsatisfactory.

An unusual case of tumor of the testicle is reported by T J Kirsin ⁵² The patient, a married man of 34 years, complained of a mass in the right side of the scrotum. There was no pain. The scrotum transmitted light, but in a manner so peculiar that the diagnosis of hydrocele was added to that of neoplasm. At operation, a teratoid growth was found and orchidectomy was done. He was treated then by deep x-ray therapy. The

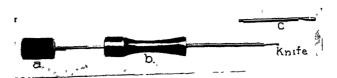


Fig 4—Ureteral carrier (divided) Note In order to free the end-piece, c, the cutting stylet, a, must be full withdrawn into the handle, b It has been pushed out subsequently in this picture in order to show the knife (Courtesy, Surgery, Gynecology and Obstetrics, April, 1937)



Fig 5—Ureteral carrier (assembled) a, Cutting stylet b, Handle c, End-piece with cup in which is tied the catgut suture which is to be cut. The stylet is partially withdrawn showing the knife (Courtesy, Surgery, Gynecology and Obstetrics, April, 1937)

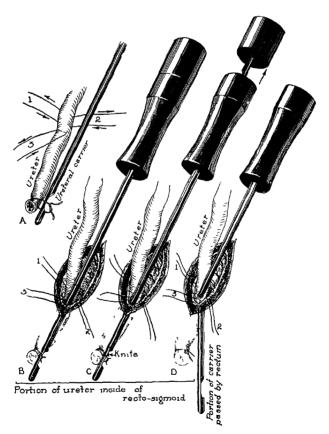


Fig 6—Illustrates the use of a divisible carrier for insertion of the end of the ureter into the lumen of the bowel A, The end of the ureter is being ligated to the fenestration in the ureteral carrier B, The end of the ureter, ligated to the fenestration in the ureteral carrier, has been introduced through an opening previously made with the cautery. The sutures, 1, 2 and 3, penetrating the submucosa of the rectosigmoid as well as the adventitia of the ureter, are tightened so as to hold the ureter in place. C, The knife of the ureteral carrier dividing the ligature which frees the end of the ureteral carrier freed within the carrier within the lumen of the bowel. D, The end-piece of the ureteral carrier freed within the rectum, when the stylet is withdrawn into the handle. The remaining portion of the instrument has not been contaminated. The anchoring sutures 1, 2 and 3 are drawn taut and tied, sealing the opening in the mucosa and submucosa (Courtesy, Surgery, Gynecology and Obstetrics, April, 1937)

patient died 11 weeks after he was first seen Necropsy showed metastases to the lungs, liver, brain, kidneys, thyroid, jejunum, ileum, large intestine, and mediastinal and retroperitoneal lymph nodes. The teratoma was classified as a chorioepitheliomata and the metastatic nodules were of the same type. This is a

many others who have worked in this particular field

F. Hinman⁵³ offers a modification of the old Coffey technic which allows a simple aseptic method of submucosal implantation of ureter into the rectosigmoid. The special part of this technic which is different from most of the



Fig 7—The method of inserting the ureter with the probe through the opening into the bowel made by the cautery. After the ureter is inserted, the mosquito clamps with rubber guards, which are not shown in the illustrations, on the loops of 1, 2 and 3, are withdrawn and these sutures are drawn taut and tied, thus anchoring the ureter in position. (Courtesy, Surgery, Gynecology and Obstetrics, April, 1937)

rather unusual type of testicular teratoma and demonstrates clearly that while such tumors are common in the female generative organs, it is very unusual to find one involving the testicle.

URETER

Ureterointestinal Anastomosis

The latest development in ureterointestinal anastomosis is, of course, a modification of the surgical procedures that have been developed by Coffey and others is the instrument for inserting the ureter into the bowel

The instrument for inserting the ureter in this manner has three parts (Fig 4), namely, the cutting stylet, a, the handle, b; and the end-piece, c, which, when assembled, form a stiff carrier (Fig 5). The end of the ureter from two to four centimeters beyond the line of anchoring sutures, according to the excess length of ureter available, is tied to the back of the carrier opposite the cup with No 2 plain catgut so that the ligature lies in the

cup and will be cut when the stylet is withdrawn (Fig 6, A). The excess length of ureter is removed by an oblique division with the cautery as close to the suture as possible, or, if cut, the end is treated with carbolic acid and alcohol The end of the ureter thus fastened to the end-piece of the carrier is now ready for insertion.

The area of submucosa to be punctured is mobilized by traction on the submucosal loops, the incision is made and the carrier, with the ureter fastened to it, is inserted through this into the lumen of the bowel in the same manner as by the method with the probe and cautery, using the carrier in place of a probe (Fig 7 and Fig. 6, B) The three anchoring sutures are drawn close but not tied Gentle traction on them holds the ureter in place until after the carrier has been removed, when they are tied Holding the handle of the carrier firmly with one hand, the cutting stylet is withdrawn with the other and one feels, with the first pull, the division of the ligature (Fig 6, C) The end of the carrier is felt now to be entirely free of the ureter The cutting stylet is kept at this point for a moment and the instrument is pushed on in until the visible portion of the end-piece is seen to be just outside the level of the submucosa, then the cutting stylet is withdrawn into the holder, which at once releases the holding joint between it and the end-piece. The end-piece drops off into the bowel, the stylet with the holder (which never should be allowed to reach the submucosa) is laid aside. and the anchoring sutures are tied When the procedure has been carried out properly, there can have been no contamination of the intestinal wound Any contamination that occurs comes from leakage at the time of tying the anchoring sutures, or afterward. This emphasizes the importance of the preparation of the

bowel by the prolonged nonresidue diet and the series of enemas beforehand with thorough syphoning off of the last one, and of careful attention to placing the anchoring sutures at the operation They must stitch the intestinal submucosal and ureteral adventitial layers only. in order to avoid the formation of a fistula They must be spaced properly in the submucosa and symmetrically opposite on the ureter so that, when they are tied, a snug implantation without looseness or constriction is secured, in order to prevent leakage and avert urinary obstruction afterward Also the puncture wound of the submucosa must be of sufficient size, but not too large

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RADIOLOGY

X-RAYS—X-RAY DIAGNOSIS

By Robert Shoemaker, 3rd, MD

DISEASES AND INJURIES OF THE SKULL

In reviewing the roentgenography of the skull, W H Caldwell pointed out that good x-ray films taken in standard positions may be of great help to the physician in the diagnosis of anencephaly, hydrocephalus, meningocele, microcephaly, oxycephaly, and bone diseases such as cramotabes, rickets, osteitis deformans, osteitis fibrosa cystica, Paget's disease, Leontiasis ossium, multiple myelomatosis, periostitis, osteomyelitis and syphilitic osteitis

Fractures of the skull may appear in the radiograph as linear cracks, depressed portions of the bone, or detached areas of the bone Primary neoplasms in the cranial bones are uncommon, but metastases are much more frequent, especially from carcinoma of the breast and thyroid The outline of the sella turcica is examined in suspected pituitary disease and the position of the pineal gland may help in locating cerebral tumors Ventriculography is an aid in the determination of hydrocephalus and certain kinds of cerebral tumors Lipiodol may be injected into various sinuses to demonstrate the presence of polypi and other protruding masses The commonest use of roentgenography of the skull is in the examination of the mastoids and sinuses

The Reliability of the Roentgenographic Signs of Intracranial Tumor

Sosman¹ has reported upon the roentgenographic examinations of the skulls of 939 patients during the last year of Harvey Cushing's service at the Peter Bent Brigham Hospital in Boston The x-ray studies usually were made before complete histories had been taken and before all the clinical studies had been finished The film reading was therefore unbiased and did not attempt to read into the films findings to agree with clinical findings The roentgenologist who read the films also wrote down his impressions of the case and signed his name From the medical service of the hospital in which there were 1900 admissions, 413 patients were sent to the x-ray department for study of the skull In this number there were 18 cases of biain tumor, subsequently verified by operation Of this number 12 were correctly diagnosed for type of tumor by the roentgenologist By clinical signs alone 11 were diagnosed for location and three for type of tumor In this group then the roentgenologist diagnosed brain tumors slightly more accurately from his films than the physicians did from their clinical findings

In Cushing's Neurosurgical Service there were 363 patients studied by roent-genography. In this group 157 patients were found to have intracranial tumors. The roentgen examinations were usually done on the day the patients were admitted. The neurosurgeons studied the x-ray films along with various other forms of evidence in deciding upon the preoperative diagnosis. The author points out especially that all departments contributed as much help and information as possible and by mutual cooperation increased the value of the

teamwork which is so essential in any complicated field of diagnosis. In this group of 157 cases of verified intracranial tumor the roentgenologist diagnosed the location of the tumor correctly in 73 cases or 47 per cent. The preoperative diagnosis by the neurosurgeons was correct for location in 135 or 86 per cent of the cases. In six cases (three per cent) the x-ray films were misleading instead of helpful

Ventriculography proved to be the most accurate technic for locating intracranial tumors. It was employed 116 times in this series. Tumors were located correctly in 59 or 95 per cent of the 62 cases verified by subsequent operation. The author goes into further detail regarding the number of pituitary adenomas, meningiomas, acoustic neurinomas, cerebellar tumors and gliomas which could be diagnosed by the x-ray examination.

SERIAL ROENTGEN EXAMINATIONS OF THE CHEST IN UNIVERSITY STUDENTS

Pohle, Paul and Beatty² have made roentgenograms of the chests of 2719 students in the University of Wisconsm in an attempt to discover early cases of pulmonary tuberculosis. Previous investigations by other authorities, in which groups of school children, students, state police, soldiers and sailors have been examined systematically by roentgenograms have demonstrated the fact that a small percentage of active tuberculous lesions were found which could not be detected by physical examination.

A questionnaire was sent to 12 leading roentgenologists to get an expression of opinion as to whether or not fluoroscopy would suffice in such an investigation. Eleven out of the 12 declared that beginning tuberculous lesions

DISCUSSION OF RESULTS

TABLE 1-SUMMARY OF X-RAY FINDINGS

| Year | Neg | Ghon | Hılum | Ghon and Hilum | Adult Inf | Apical Pleur |
|----------------------|-------------------|----------------|----------------|----------------------|----------------|-----------------|
| 1934 1935 1936 | 507 752 813 | 66 93 73 | 47 64 69 | 33 51 75 | 16 11 18 | 10 2 19 |
| Total | 2072 | 232 | 180 | 159 | 45 | 31 |
| Per cent | 76 21 | 21 | | | 2 79 | |

(Courtesy, Radiology, January, 1937)

TABLE 2-X-RAY FINDINGS NOT RELATED TO TUBERCULOSIS

| Year | Heart | Anom Lobes | Anom Ribs | Pleural Thick | Chron Infl | Bronchi- ectasis | Rıb Res | Misc |
|----------------------|----------------|---------------|----------------|------------------|---------------|---------------------|------------|------|
| 1934 1935 1936 | 26 48 48 | 6 9 7 | 17 18 14 | 17 32 24 | 5 21 | 2 | 2 | 3 2 |
| Total | 122 | 22 | 49 | 73 | 26 | 3 | 2 | 5 |

(Courtesy, Radiology, January, 1937)

in the lungs can not be detected by fluoroscopic study as early as by good roentgenograms of the chest One good authority put this in the following words "It is simply optically and physically impossible for the fluoroscope to detect changes in densities as accurately as can be done by the film" In regard to following the progress of tuberculous lesions another authority had the following to sav "A man would have to have a wonderful memory to be able to say that a faint shadow is more faint or less faint now than it was six months or a year ago To depend upon the fluoroscope for the diagnosis and followup of early tuberculosis or any phase of tuberculosis, would be to turn back to the days before radiographs were made No roentgenologist would do it, and any other physician who did should not be permitted to practice medicine"

The authors decided the evidence was overwhelming in favor of the use of films rather than fluoroscopy. Paper films were not considered practicable because they do not show sufficient fine detail to reveal minimal tuberculous lesions ³

With the facilities at hand it was deemed impossible to take x-ray films of all the 2000 to 2500 new students enrolled each year in the University of Wisconsin The Student Health Service consequently did Mantoux tests first All of the positive reactors were then referred for the roentgen examination

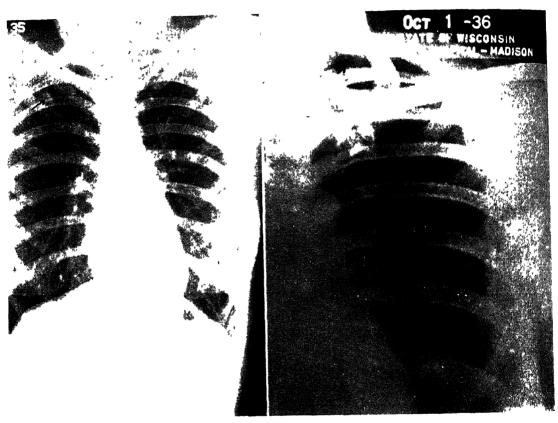
Technical Procedure—The technical procedure adopted is given in the author's own words

"Since the examination of such a large number of individuals would add a considerable burden to a busy department, a method was worked out whereby these examinations could be done in a minimum of time and without interfering too much with the routine work

"Groups of approximately 100 students were examined at a time, the work be-

ginning immediately after regular hours Men and women were taken in separate groups All clothing was removed to the waist, the women were given paper jackets to wear The group was formed in line passing by a desk where two persons took care of the handling of records and the preparation of identifi-

the dark room By proper team work it was possible to make an examination approximately every 45 seconds and a group of 100 could be handled in about one hour. In spite of the rapidity with which the examinations were done there were only three per cent retakes needed due to improper technic. Only one skilled



 $F_{1g} \quad 1 \qquad \qquad F_{1g} \quad 2$

Fig 1—Adult type of tuberculosis in lung parenchyma Fig 2—Apical pleuritis (Courtesy, Radiology, January, 1937)

cation numbers. The technical procedures concerned with the exposing of the films were handled by three persons. One technician positioned the patient before the film holder, measuring the thickness of the chest, gave the necessary instructions to the patient, and instructed a second technician handling the controls as to the proper voltage to be used. A third assistant carried the cassetts to and from

technician was necessary, the rest of the work could be done by less skilled helpers. The loading and unloading of cassetts in the dark room required the services of two persons. Exposed films that could not be developed immediately were stored in light-proof boxes and processed later. The technical factors used were as follows distance, 72 inches (1828 m), 150 milliamperes, time of

one-tenth second, voltage varied according to the thickness of the chest"

The results of examinations conducted in the years 1934, 1935 and 1936 are shown in Table 1 and Table 2. The second column of Table 1 shows the number of cases with no evidence of tuberculosis, 76 per cent of all students

last two columns include the cases showing evidence of the reinfection or adult type of lesion. These were subdivided further into those in which the lesion was in the lung parenchyma (Fig. 1) and those in which the major change appeared to be a thickening of the apical pleura (Fig. 2) (Nearly three per cent

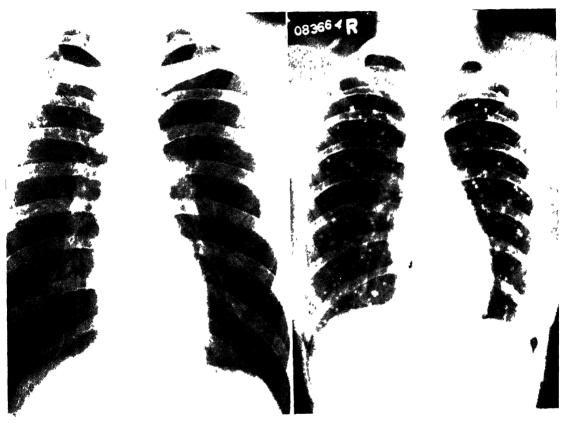


Fig 3

Fig 4

Fig 3— Advanced adult tuberculosis with cavitation Fig 4—Multiple calcified hematogenous foci (Courtesy, Radiology, January, 1937)

examined by roentgenograms. The next three columns give the number of cases showing calcification, either in the lung parenchyma (Ghon tubercle), in the hilum lymph nodes, or in both. The presence of such calcification was considered evidence of a previous first infection or childhood type of tuberculosis (Twenty-one per cent were found to belong in this general group). The

of the students showed these adult type lesions)

The authors consider apical pleuritis in this age group to have more significance than in patients of more advanced age. In order to be classed as tuberculous apical pleuritis a band of increased density, over the summit of one or both apices, had to show a rough and irregular lower margin. In some

roentgenograms fine trunk markings could be traced up to and merging with the band of increased density. Progress films at suitable intervals are indicated in some of these cases as it was found to be difficult to determine whether the lesion was confined to the pleura or whether there was involvement of the subjacent lung parenchyma Progress films helped in deciding whether the

In one student multiple calcified hematogenous foci were found as shown in Fig 4. An unusual accidental finding is illustrated in Fig 5, where there was a metastatic nodule in the lung parenchyma from a primary carcinoma of the breast

In Table 2 are listed some of the abnormalities discovered which were not related to tuberculosis. Among these of



Fig 5—Metastatic carcinoma in lung parenchyma (Courtesy, Radiology, January, 1937)

thickening was of recent inflammatory nature or was older and consisted of fibrotic scar tissue

Nearly all types of tuberculosis were discovered Some were unquestionably active, as evidenced by the softness of the shadows, and some were so far advanced as to show cavitation as illustrated in Fig 3 In regard to the extensiveness of the involvement it was found that some lesions were evidenced by small round or wedge-shaped opacities while in other cases half of both lungs was diseased

definite clinical importance is bronchiectasis, while abnormalities of the heart, thickened pleura, and resected ribs might in some cases have significance

It appears to the reviewers that the authors have done an extremely creditable piece of investigation. They have shown that in a large group of young people, presumably healthy enough to carry on the strenuous work of college life, there is about one in every 100 who has definite signs of active or quiescent adult type of pulmonary tuberculosis. It would appear well worth the time and

money spent if similar investigations could be extended to other groups of young people Early discovery of disease might go a long way in the saving of life and reducing the incidence of tuberculosis

URETERAL STONE

Roentgen Analysis of 100 Cases—Peterson and Holmes⁴ investigated 100 cases of ureteral stone in which the original roentgen report had indicated the presence of calculus in only 79. In a larger series Bumpus and Thompson had visualized the stone in the x-ray film in 98 per cent. This high percentage was attributed to the fact that the urologist who was aware of the clinical findings, interpreted the films

Peterson and Holmes then, with all the clinical data at hand, restudied the films of their 21 cases previously reported negative. In this investigation calculi were found in all but four, thus bringing their correct interpretations up to 96 per cent.

A chart was then made showing the location of the stones, 80 per cent being 111 the pelvis and 66 per cent in the extreme lower end of the ureter. Exanimation of this chart reveals the fact that this 66 per cent of stones lie just above a line joining the extreme bases of the ischial spines Anatomically this line corresponds approximately with the lowest level of the intramural section of the ureter One large stone found to lie just below this line was situated in a ureterocele prolapsed into the bladder The probable explanation for the high percentage of stones found here is that the intramural section of the ureter is more rigid than other sections and refuses to dilate to allow the passage of calculi

In making roentgenograms the x-ray tube should be centered at the level of

the iliac crests and should be angulated towards the feet so that the central ray is projected along the pelvic axis. If the tube is centered directly over or below the pelvic inlet the resulting roentgenogram will show a flattened bony pelvis in which the ischial spines may be projected on the same level with or below the upper margin of the superior ramus of the pubis. Such a picture might be confusing because the lower ends of the ureters lie at this same level and hence a stone in this region may be projected onto the pubic bones, especially if the bladder is not distended

Peterson and Holmes discovered an interesting association on correlating the clinical history and the size and location of calculi. All patients with large calculi in the lower end of the ureter had urinary symptoms of long standing. The roentgenologist may predict on seeing a large stone in the lower ureter that the patient has been ill for some time and that the present attack of ureteral colic is not the initial one. Likewise, a small calculus in this location usually means an acute attack of a few hours to a few days in duration.

HYSTEROSALPINGOGRAPHY IN GYNECOLOGIC DIAGNOSIS

Many of the pathologic conditions with which the gynecologist must contend involve the cavities and limings of the uterus and tubes, and hysterosalpingography offers the best and simplest means of locating and estimating the extent and severity of these conditions

Mathieu⁵ has gained experience from more than 1200 injections of iodized oil and is convinced that hysterosalpingography, when properly carried out, is safe and is only a minor procedure from the

patient's standpoint In all these examinations there have been no catastrophies

The contraindications are active, serious infection of the genital tract and normal pregnancy

In making the injection of iodized oil strict aseptic and antiseptic precautions should be observed. The technic is sim-



Fig 6—Hysterosalpingography (Courtesy, Radiology, April, 1937)

ple and is given in detail by the author

"The patient is placed in lithotomy position over a Bucky diaphragin at the end of a table which has stirrups A good light reflected into the vagina is necessary A vaginal speculum is inserted, and the vagina and cervix are cleaned of discharge Tincture of iodine is applied to the cervix and to the external os The anterior lip of the cervix is then grasped with a single tooth volsellum to hold it in a fixed position The oil-filled, short-tipped cannula, attached to the syringe, is inserted into the external os, pressing the acorn of the cannula gently against its opening, and the oil is injected slowly into the uterine cavity When the cavity is filled

the oil will proceed into the tubes if they are patent At this time the patient will experience painful uterine contractions, and the oil will leak backward between the acorn of the cannula and the cervical opening The amount of oil required for the injection is usually from (more, however, if the 5 to 8 cc uterine cavity is large, and less if it is small) The amount of pressure used in the injection should be scarcely more than that used in giving any injection through a syringe By observing this precaution there can be no danger of excessive pressure Once the cavity is filled, the roentgenogram is made with the cannula still in position, then the cannula is removed and the oil is allowed to run from the ceivix This completes the injection which, with exposure of the film, usually takes two minutes after the vaginal speculum has been inserted By using the short-tipped cannula (Fig 6), the position of the uterus or the direction of the canal need not be known. and sounding of the uterus is unnecessary since the short-tipped cannula does not extend to the internal os

"It is always well to describe the technic to the patient, and to advise her that she will be told in advance of each pain—that associated with the grasping of the anterior lip with the volsellum, and that associated with the insertion of the cannula, and that associated with the filling of the uterine cavity. When she is so advised, and is told further that the entire procedure will be over in two minutes, her discomfort is lessened, expectation of severe pain is prevented, and co-operation is assured.

"Another roentgenogram should be taken from 8 to 24 hours later if one wants to know about the patency of the tubes By this time the tubes and uterus will be empty of the oil, and if the tubes

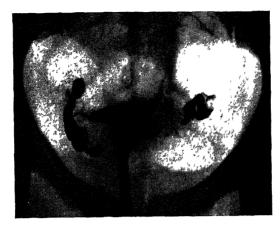


Fig 7-Hysterosalpingogram of normal uterus and tube Note triangular shape of uterine cavity without filling defects, normal proximal two-thirds of tubes, and dilated distal ends with partial spill of oil (Courtesy, Radiology, April, 1937)



Fig 9 Fig 8

 F_{1g} 8—Stricture of the internal os Fig 9—Localized hyperplasia in the region of the internal os

(Courtesy, Radiology, April, 1937)



Fig 10—Generalized hyperplasia of the endometrium (Courtesy, Radiology, April, 1937)



Fig 11—Filling defect caused by polyp of the uterine cavity (Courtesy, Radiology, April, 1937)



Fig 12 Fig 13

Fig 12—Polyp of the uterine cavity projecting down from the fundus
Fig 13—Several small fibroids on the posterior surface of the lower segment of the uterus,
causing bulging and dilatation of the lower segment of the cavity

(Courtesy, Radiology, April, 1937)



Fig 14—Bicornuate uterus Roentgenogram made vertically through the fundus (Courtesy, Radiology, April, 1937)

are patent there will be some filmy traces of oil in the pelvic cavity. In the cases in which the tubes are closed, the actual site of the closure will be seen in the cornu, in the tube proper, or at the distal extremity. All the cavities of the uterus

defects. The fine, hazy, tortuous shadow of a Fallopian tube extends from each upper horn of the uterine cavity. The distal third of each tube is distended to three or four times the diameter of the proximal two-thirds



Fig 15—Sagittal section through uterus and tubes of Fig 14 (Courtesy, Radiology, April, 1937)

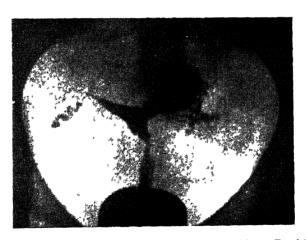


Fig 16—Missed abortion in horn of bicornuate uterus Aschheim-Zondek test negative, (Courtesy, Radiology, April, 1937)

and tubes reached by the oil will be visualized with the roentgen ray"

Figure 7 shows the hysterosalpingogram of a normal uterus and tubes. The uterine cavity is smoothly outlined and approximately triangular and the cervical canal is open and free from filling Figures 8 and 9 illustrate deformities of the cervical canal, which may be identified as stricture of the internal os and localized hyperplasia in the region of the internal os Other deformities such as kinks, obstructions and dilatations are readily demonstrated

Figure 10 shows generalized hyperplasia of the endometrium

Figures 11, 12 and 13 show filling defects due to polyps and fibroids

Figures 14, 15, 16, 17 and 18 show double uterus in several forms and illus-

cavity is demonstrated by the iodized oil it is proved definitely that pregnancy is not in the uterus

The author has established what appears to be a pathognomonic sign for certain cases of adenomyoma of the



Fig. 17—Sagittal section through bicornuate uterus containing abortion in horn of Fig. 16 (Courtesy, Radiology, April, 1937)



Fig 18—Double uterus Patient had two vaginae and two cervices Note evidence of bilateral hydrosalpinges (Courtesy, Radiology, April, 1937)

trate how congenital anomalies may be revealed by hysterosalpingography. It is often invaluable in the diagnosis of ectopic pregnancy for if a small uterine

uterus In those cases in which there is an infolding of the endometrium in such a manner as to make long, cryptic tubes, dipping deeply into the myometrium, the 10dized oil will penetrate these cryptic tubes which will then be beautifully visualized This is the only situation wherein oil can be seen penetrating a myometrium in this characteristic manner, as shown in Figure 19

normal tube has a characteristically fuzzy appearance, while the lumen of a chronically diseased tube will have a sharply outlined, wiry appearance as shown in Figure 20 In differentiating between a tubal mass and an ovarian

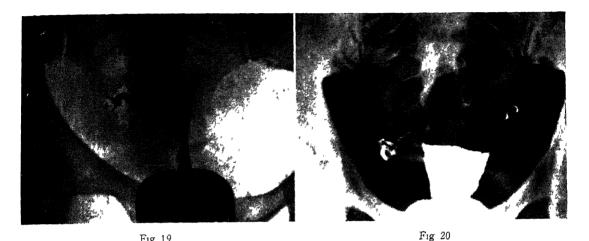


Fig 19-Adenomyoma of the uterus Note iodized oil in crypts formed by infolding of endometrium into the myometrium Fig 20-Note the wiry appearance of chronically diseased tubes with the absence of normal

distal dilatation. (Courtesy Radiology, April, 1937)

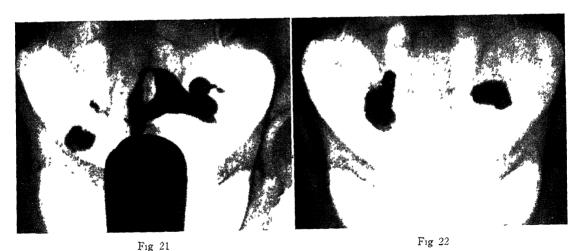


Fig 21—Bilateral hydrosalpinges Note sacculated dilatation at extreme end of each tube Fig 22-Film taken 24 hours after Fig 21 Note bags of oil (Courtesy, Radiology, April, 1937)

tubes is one of the most helpful aids distal extremity it can be excluded as to diagnosis which can be derived from the site of the mass Small hydrosalhysterosalpingography The lumen of a pinges which cannot be detected with

The patency or non-patency of the mass, if the tube fills normally to its

bimanual examination are often revealed by hysterosalpingography. In about 50 per cent of these small hydrosalpinges the cornual ends of the tubes are open and allow oil to enter, and the configura22) The 24-hour film shows the uterus and the proximal two-thirds of the tubes empty and free of iodized oil but the shadows of the distal ends of the tubes are the same as they were the



Fig 23 Fig 24

Fig 23—Bilateral hydrosalpinges Note sacculated dilatation at end of each tube
Fig 24—Film taken 24 hours after Fig 23 Note iodized oil retained in sacculated ends of tubes

(Courtesv, Radiology, April, 1937)

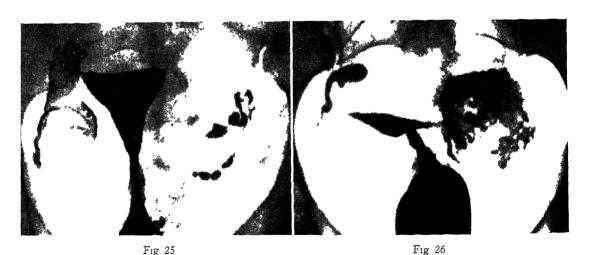


Fig 25—Ectopic pregnancy aborting from the distal end of right tube. Note how oil drapes itself about the aborting mass.

Fig 26—Ectopic pregnancy aborted from distal end of left tube. Note how oil drapes itself about the aborted mass (Courtesy, Radiology, April, 1937)

tion of the tubes shows in a characteristic manner. In the film taken at the time of injection the tubes have the appearance previously described as characteristic of normal tubes (Figs. 21 and

day before (Figs 23 and 24) If another film is taken a week or two later the same bags, or shadows, unchanged will be seen. Tubes in normal healthy condition empty by peristaltic action but

portions of the tube which have been dilated excessively in the case of hydrosalpinx have thinned and weakened musculature which cannot function and empty.

Figures 25, 26, 27, and 28 show how hysterosalpingograms can aid in estab-

lishing the diagnosis and even the exact site of ectopic pregnancy. The author states that injection of iodized oil into the uterus and tubes in a case of tubal pregnancy is practically harmless when done carefully by a person experienced in this procedure



Fig 27 Fig 2

Fig 27—Ectopic pregnancy in the midportion of left tube. Note how tube ends abruptly in a rounded manner just proximal to the tubal pregnancy. Note filling defects at each end of uterine cavity. These are due to filling defects caused by decidua. This roentgenogram does not visualize the ectopic pregnancy. It merely visualizes the characteristic finding in that portion of the tube proximal to an ectopic pregnancy in the midportion of the tube.

Fig 28—Ectopic pregnancy in the right tube. Note how tube ends abruptly in a rounded manner just proximal to the tubal pregnancy. This roentgenogram does not visualize the ectopic pregnancy. It merely visualizes the characteristic finding in that portion of the tube proximal to an ectopic pregnancy in the midportion of the tube.

(Courtesy, Radiology, April, 1937)

RADIUM AND X-RAYS IN THERAPY

By Robert Shoemaker, 3rd, M D

CANCER

Principles Governing Radiation Therapy—In a discussion of the treatment of cancer by irradiation, G T Pack⁶ states that surgery, the actual cautery, and chemical cauterization agents all have their place in removing or destroying cancerous tissues Radiation therapy, by x-rays and gamma rays from radium has definite advantages over these

other methods in cases of cancer, in which the cancer cells are more easily killed than are the cells of the normal surrounding tissues. Radiosensitivity seems to have some relationship to the origin of the cells making up the cancer. Tumois developing from primitive blood-forming tissues are likely to be radiosensitive, as for example, lymphosarcoma, myeloma, endothelioma and angioma. Tumors de-

veloping from neural crest cells are likely to be radioresistant, as for example, glioma, neurosarcoma, melanoma and mixed tumor of the parotid

Methods of Radiation Therapy. Irradiation therapy may be applied by two methods:

- (1) From an external source
- (2) From a source applied directly into the tumor or surrounding it

External radiation may be given by x-rays with low voltage for superficial lesions and with high voltage or supervoltage for deeply seated lesions Radium may be used instead of x-rays for the treatment of superficial lesions by means of small plaques, trays or moulages Radium may be used for deeply seated lesions (teleradium therapy) by means of large quantities of radium in bombs or packs several centimeters away from the lesions under treatment

Intracavitary Irradiation—Radium element in tubes, covered with sufficient platinum, gold, brass or aluminum for filtration, may be placed within body cavities for contact treatment of cancers of nares, orbits, antra, larynx, esophagus, uterus or vagina

Interstitial Irradiation — Radium needles and radon seeds may be driven directly into or placed in groups surjounding cancers in soft tissues. This method of treating accessible tumors is usually supplementary to external irradiation.

Units of Dosage—Pack has summed up the subject of dosage used in irradiation therapy concisely in the following words "It is best to administer to all the neoplastic territory the maximal quantity of radiant energy compatible with the maintenance of tissue integrity. To speak intelligently of these quantities it is best to have some common physical and biological measures of the dosage. Thus in the case of radium the quantity of gamma

rays at the source is known as the "dose of emission." One knows with precision the dose of emission because this is invariable. The dose emitted is expressed by two different notations The one has for its basis the intensity of the gamma rays and the duration of their application; the intensity is proportional to the quantity of radium present; the dose is obtained by the product of the quantity and the time, which is expressed as milligramhours of radium or as millicurie-hours of radon (gram-hours or curie-hours in the case of large radium bombs or packs) The other notation, which is utilized throughout France, makes the dose proportional to the quantity of radium emanation destroyed (disintegrated) during the course of its application This is expressed in terms of "millicuries-destroyed" or of "microcuries-destroyed," the latter term connoting only one-thousandth of the former The physical efficiency of one millicurie of radon throughout its life is equivalent to 133 millicurie-hours Therefore one nullicune-destroyed is equivalent to 133 millicurie-hours or 133 milligram-hours

The dose of gamma or roentgen rays at the surface or the point of entrance into the body is the superficial dose while the dose to the tumor by unit volume of the tissues treated is the "tissue or tumor dose"

The unit of x-ray dosage called the "roentgen" or "r" (designated always by small "r") has been standardized and internationally accepted. The roentgen has been defined as that quantity of roentgen radiation which, when the wall effect of the ionization chamber is avoided and the secondary electrons are fully utilized, produces in one cubic contimeter of atmospheric air at 0° C and 76 cm mercury pressure such a degree of conductivity by ionization that

one electrostatic unit of charge is measured at saturation current

"In the measurement of roentgen rays and gamma rays by biological means, the most common unit is the establishment of an erythema dose under certain conditions Quimby of the Physics Department of the Memorial Hospital has defined and employed the term 'threshold erythema,' which is that dose of radiation that will cause a perceptible change in the skin of 80 per cent of the subjects and no discernible discoloration in 20 per cent in two to four weeks after the exposure to the rays Quimby has found that the threshold erythema with 200 Kv, 100 sq cm field, 50 cm targetskin distance, and filter of 05 cm copper and 25 cm aluminum is 500 to 525 roentgens The therapeutic erythema, on the other hand, varies with different radiologists from 600 to 1000 roentgens"

The Tissue Dose - Cancericidal Dose - At the Memorial Hospital the "threshold erythema," is used as the unit of tissue dosage As mentioned above, this can be determined for each x-ray tube and each radium applicator by direct experiment At various depths below the surface of the tissue being irradiated the depth doses can be calculated as being various percentages of the dosage of the radiation falling on the surface method of determining these percentages is by making measurements with a small ionization chamber placed first on the surface of a vessel of water and then placed successively at various depths below the surface of the water Such water phantom measurements agree fairly well with measurements obtained by placing the ionization chamber similar distances beneath the surface in various cavities in the human body. The data obtained by these water phantom measurements are plotted as "isodose curves" These isodose curves are used for rapid calculation of the depth dosage given to a tumor when irradiated by cross-firing through several portals

In cases of interstitual irradiation the measurement by direct experiment is more complicated especially as the irradiation is applied from numerous sources simultaneously. At Memorial Hospital this has been worked out in a practical manner by Martin and Quimby They have demonstrated that in any sphere it makes little difference in the dosage at the periphery whether the source of radiation be concentrated at the center or be distributed uniformly within the inner half of the sphere They have prepared tables for spheres of various sizes giving threshold erythema dosages at the periphery when various quantities of radon are placed near the center or at least within the inner half of the spheres The cancericidal doses for many different kinds of tumors have been determined by actual clinical observation and can be stated in terms of threshold ervthema dose (T E D) For example intraoral squamous cell carcinoma requires 6 to 8 T E D, while transitional cell carcinoma requires 2 to 4 T E D for sterilization By calculating external irradiation and interstitual irradiation in terms of the same unit it is convenient then to determine combined external and interstitial irradiation by adding the number of units applied in the two methods

Prescription for Roentgen Therapy—For the safety of the patient roentgen-ray dosage must be prescribed in an accurate way and a detailed record should be kept of the treatment given The quantitative factor should be expressed in r units and the qualitative factor in Angstrom units or by stating the half-value layer in millimeters of copper, aluminum or other metallic filters. In addition to these two factors should be specified the kilovoltage, filtration, tar-

get-skin distance, and time of application in minutes. The tumor depth below the surface should usually be indicated. The size and number of the portals through which treatments are given is also important as is also the factor of number of treatments and the intervals between treatments for a single massive dose has an effect quite different from that of the same total dosage fractionated over several weeks or months.

Kilovoltage (Potential) - As the voltage or potential applied to the x-ray tube is increased, the average wave length of the rays emitted becomes shorter and shorter Short waves penetrate tissues more readily than longer waves. This important factor is utilized in therapy of tumors deep below the surface by applying high voltages of 200 Kv to 1000 Kv For therapy of superficial skin diseases lower voltages are used All x-ray tubes give off rays varying considerably in wave length When the effect of short waves on deep tumors is desired filters of copper, aluminum or other metals, are employed, to absorb the long waves which would have an undesirable effect on the skin and superficial tissues

Comparison of Teleradium Therapy with Supervoltage Roentgen Therapy - It has been estimated that supervoltages of over 1500 Kv would produce x-rays having wave lengths comparable to the gamma rays of radium Already there are several 1000 Kv or million volt machines in use in the United States The roentgen rays produced by these machines have biological effects differing little, if any, from the effects which follow teleradium therapy with packs containing four grams of radium The roentgen rays have far greater intensity and so can be used to treat more patients in a given time. This greater intensity may not be desirable, however, for therapy spread out over a longer period seems to have advantages

Effective Wave Length of Radiation—The wave length of roentgen rays depends upon two factors. The velocity with which the electrons fly across the x-ray tube and bombard the target and the atomic weight of the material of which the target is composed The velocity with which the electrons fly across the tube increases with the voltage applied to the terminals of the tube The wave length of the roentgen rays becomes shorter as the voltage is increased The higher the atomic weight of the target material the shorter the wave length of the roentgen rays emitted Tungsten, of which most targets are made, has a very high atomic weight and emits characteristic rays of very short wave length When roentgen rays emitted by the tungsten target enter the human body they encounter secondary targets of much lower atomic weight such as sodium, potassium and calcium The secondaiy rays given off from these targets have much longer wave lengths and feebler penetration than the original rays It is apparent that the way to get deep penetration, to deliver greater depth dosages, is to raise the voltage applied to the x-ray tube To put this into figures, Pack gives the following

"Failla has found that the relative depth doses of 10 cm depth obtained under comparable conditions with 200 Kv roentgen rays, 700 Kv roentgen rays and gamma rays, are respectively 290, 412 and 567 per cent Accordingly from this point of view 700 Kv roentgen rays are considerably better than 200 Kv roentgen rays, but not as good as gamma rays. This advantage is not realized in clinical practice because it is not practical to apply radium at the focal distances used in roentgen therapy"

Ionization in Tissues—The destruction of living cells by radiation is due to the release of electrons from the atoms, of which the cells are composed, when these atoms are bombarded by gamma rays or roentgen rays Finally, the atoms, minus one or more electrons, combine with other electrons In some cases the recombination is harmless to the cell but in other cases the recombination is a form of chemical change which brings about the death of the cell

Current (Milliamperage) — The kilovoltage applied to the terminals of the x-ray tube determines the speed with which the electrons fly across the tube and strike the anode and determines the wave length of the x-rays emitted In a similar manner the milliamperage is an indicator of the number of electrons flying across the tube. The more electrons flying across the tube the more x-rays are emitted from the anode in a given length of time. Pack states this concisely in the following words.

"The usual roentgen tubes carry from 4 to 30 milliamperes Thus a tube running at four milliamperes for 25 minutes would deliver 100 milliampere-minutes and a tube running at 25 milliamperes for four minutes would also deliver 100 milliampere-minutes or its equivalent in identifiers, other conditions remaining the same"

Filter—As previously mentioned, high frequency roentgen rays, which have short wave lengths, penetrate more deeply into the body tissues before their energy is expended than do roentgen rays of lower initial frequency and correspondingly longer wave lengths Conversely low frequency roentgen rays, which have long wave lengths, expend their energy on the skin or superficial tissues and do not penetrate to the deep tissues. When tumors far beneath the surface are to be treated it is necessary to interpose

filters of copper, aluminum or other metals to absorb the rays of long wave length and thus protect the skin and superficial tissues The waves of short wave length pass through copper and other metals if the filter is comparatively thin The number of millimeters of copper or other metal which will cut down the intensity of an x-ray beam to one half of its initial intensity is called the "half-value layer" It is an indicator of the quality or wave length of the beam Another way of expressing the effective wave length of the beam is to give the measurement in Angstrom units The author gives the following data to illustrate.

"Failla and Quimby have found that the effective wave length employed in the usual deep roentgen therapy at the Memorial Hospital is about 0.16 Å. This treatment is given with 200,000 volts (peak) filtered by 0.5 mm. Cu. and 1 mm. Al. With intermediate voltage of 140 Kv. the filter may vary from nothing up to 6 mm. of aluminum, with a filter of 4 mm. Al. the effective wave length is about 0.25 Å.

"In the case of radium the filters employed, brass, lead, silvei, gold or platinum are usually expressed in the equivalents of certain thicknesses of platinum One millimeter of platinum or its equivalent (occasionally 0.5 mm platinum) is the customary filter for surface application of radium or teleradium therapy radium treatments Intracavitary given with filters of 05 to 1 mm of platinum, while interstitial irradiation requires considerable less filtration Gold radon seeds have a wall thickness of 03 mm gold and most platinum needles for interstitial use are designed with a wall thickness equivalent to 05 mm"

Size of Field of Irradiation—When roentgen rays and gamma rays strike the human body, a portion of their energy

is absorbed by the atoms of which the tissues are composed and rays of longer wave length are given off in various directions These oblique rays in turn strike other atoms and are given off again in various directions and at still longer wave lengths After these secondary rays have struck many atoms successively the rays have been scattered in all directions and many of them are even going in the opposite direction from that of the initial rays In this manner the skin and superficial tissues are bombarded in all directions by the initial rays plus the scattered secondary rays It is quite easy to picture this mentally and to comprehend that the larger the area treated by irradiation the more the scattered rays from portions of the initial beam will overlap the scattered rays from other portions of the beam The scattered rays may amount to as much as 40 per cent of the total radiation in the skin and superficial tissues At a depth of 10 cm the scattered radiation may amount to 80 per cent if the area treated is large. This is a very important fact to be considered in planning deep therapy Large concentration of radiation in deep tumor tissues may be obtained, and at the same time skin dosage kept within the limits of toleration, by using small portals and directing the beam accurately at the tumor from several different directions

Target-skin or Radium-skin Distance—Pack has presented the distance factor so concisely that it is quoted

The inverse square law of radiation states that the intensity of a beam of roentgen rays or gamma rays varies inversely proportional as the square of the focal skin distance from a point source. Thus the radiation intensity from a high voltage roentgen tube at 50 cm distance is almost twice that delivered at 70 cm focal-skin distance. Or a radium appli-

cator placed at 2 cm radium-skin distance conceivably would deliver four times the superficial dose as the same applicator applied for the same time at twice the distance or 4 cm (This is not exactly true since the radium applicator is not a point source) This fact may be expressed also in the following manner Since the dose is dependent on the product of the intensity times the duration of exposure, the radium treatment at 4 cm distance would require four times as many minutes or hours as at 2 cm radium-skin distance The question naturally arises, why not decrease the focalskin distance as much as possible to save time and expense? In the case of verv superficial non-infiltrating skin cancers this plan is feasible but for the more deeply situated cancers the depth or tissue dose is increased (in comparison to the dose delivered to the superjacent skin and tissues) with the greater skintarget distance Theoretically, the distance might be increased sufficiently so that the relative dose on the skin at the portal of entry of the rays would be almost the same as at the location of the tumor within the body "

Heublein Method of Continuous Irradiation—The theoretical increase of target-skin distance to such great distance that the tumor dose and skin dose will be almost the same has been put to experimental trial by Heublein and Cravei at the Memorial Hospital The x-ray tube was placed 24 feet away from the patients lying in bed The tube was operated at 185 Ky and 3 ma. The time required to deliver 225 r at 24 feet was 250 hours or 12 5 days at 20 hours a day The clinical skin erythema dose of 750 r (measured in air) was the unit of dosage employed One hundred and thirty-four cases were treated in two years. These were mostly generalized and radiosensitive tumor processes, such as the leukemias, lymphosarcoma, Hodgkin's disease and multiple myeloma The results in the treatment of chronic lymphatic leukemias and pseudoleukemia seemed superior to any obtained previously by local irradiation The treatments were given cautiously at first and dosages were eventually increased to 375 r to 450 r There were no complications resulting from irradiation except the occasional development of leukopenia, anemia and thrombocytopenia in some cases This is considered to be one of the most important achievements in radiation therapy in the last decade Its principles of low intensity, great distance, continuous irradiation and long duration of treatment may be found of value in the therapy of many cancers which have been refractory to other methods

Time Intensity Factor—Satisfactory irradiation treatment in the cure of any cancerous condition involves the adjustment of dosage so that the cancer cells will be destroyed and the normal tissue cells will be allowed to live It might involve the prevention of reproduction of the cancer cells and allow reproduction of the normal cells In the latter case the cancer cells would simply die of old age, leaving the succeeding generations of normal cells in undisturbed occupancy The dosage which can be used in therapy is limited by the amount of radiation which the normal cells can receive and still continue to reproduce Regaud, Coutard and Lacassagne performed some very important experiments which allowed them to draw conclusions regarding the method of irradiation which would kill cancer cells and allow the survival of normal tissue Their test materials were rabbits in which various dosages of x-rays were administered to the testicles and ano-The rapidly rectal skin and mucosa developing spermatogonia resembled in many ways the rapidly developing cancer cells. The skin and mucous membrane were representative of normal tissue cells It was found that the spermatogonia could not be killed by a single massive dose of x-rays without at the same time causing serious damage to the skin and mucous membrane When the x-ray treatment was given in several fractional doses with a considerable interval of time between the doses then there was a great difference in effect, the spermatogonia were affected even more than by the single dose, while the skin and mucous membrane were affected less than by a single large dose Pack states this in the following manner

"Regaud's explanation of the superiority of continuous or fractionated irradiation over short intensive treatments is founded on the existence of alternating periods of radiosensitivity and of radioresistance in the life of the spermatogonia (in the experiments) and the cancer cells (in clinical practice). Spermatogenesis in a mammal such as the rabbit is a continuous phenomenon if the testicle is considered as a whole But if one considers only a certain cell or line of cells on a seminiferous tubule, the function of reproduction by cell division is seen to be discontinuous and cyclic and the spermatogonia-like cancer cells, pass through alternating phases of multiplication (brief phases) and of rest (long phases) In one line of cells, either spermatogonia or cancer cells, the phase of multiplication corresponds to accentuation of radiosensitivity (law of Bergonié and Tribondeau) whereas the phase of rest corresponds to the diminution in radiosensitivity A short treatment therefore might destroy only those spermatogonia or cancer cells which are dividing at that time, it spares the others. It is only natural that prolonged and continuous irradiation (in the case of radium) or well fractionated irradiation with

proper spacing of the fractions into a fairly long time (in the case of roentgen rays is more efficient than brief intensive radiation, because in the first case the germinal or cancer cells are killed one after the other as the cycle progresses and these cells enter for the moment the phase of maximal radiosensitivity These principles are now so generally recognized that the prolonged irradiation of low intensity or fractionated cumulative treatments have found almost universal favor with roentgenologists and radium These treatments depend usually on the administration of suberythema doses repeated every 24 or 48 hours until a total dose of six to eight threshold erythema units may be delivered to one skin portal with perfect To illustrate the application of this principle, let us consider the treatment of a hypopharyngeal carcinoma by high voltage roentgen rays only Two lateral portals are used to crossfire the beams of radiation. With a single massive dose, only 850 r can be given to each side of the neck without seriously damaging the skin By the fractionated method 300 r may be given daily alternating on each side of the neck until a total of 3000 to 4000 r are delivered through each portal Such a course of treatment requires three weeks to consummate the dose required to sterilize the caremoma"

Summary of Methods of Treatment

There are four methods of treatment commonly employed

- 1 The massive dose technic
- 2 Saturation dose
- 3 Fractionated dose
- 4 Continuous irradiation.

The single *massive dose* was formerly used and was intended to destroy all the cancer cells at once If, however, a few cancer cells survived, the cancer might

If the dosage was just grow again below the tolerance of normal tissue cells the skin and superficial tissues would survive A massive dose treatment could not be repeated for several weeks Kingery introduced the saturation dose method in the treatment of skin diseases by low voltage x-rays without any filter gave an initial erythema dose and then maintained the biological effect by adding smaller doses at proper intervals. He added 50 per cent of an erythema dose after three and one-half days to make up for the recuperation of the tissues from the initial dosage Pfahler was the first radiologist to use this method in the treatment of cancer by properly filtered high voltage x-rays

In the fractionated dose method daily treatments are given with doses below an erythema dose. A cumulative effect is obtained. The cancer cells do not recuperate as quickly as normal cells from irradiation and so a cancericidal cumulative dose is reached before a cumulative dose, lethal, to normal tissue cells is reached. Also, as mentioned previously, the irradiation given in repeated dosage is more likely to destroy the rapidly multiplying cancer cells during their periods of cell division.

The continuous method of irradiation, as used by Heublein and Craver with their teleroentgen equipment, is a further development of the method of fractionated small dosages. Treatment is given for 20 hours a day for several weeks with x-ray tubes 24 feet away from the patients

The Biological Action of Neutron Rays

Lawrence⁷ describes the cyclotron by means of which he produces neutron rays by bombarding a beryllium target with high speed deuterons. Neutron rays are really streams of tiny particles knocked out of the nuclei of the beryllium atoms Each neutron consists of a proton and an electron in intimate association so that the positive electric charge of the one exactly neutralizes the negative charge of the other. Such neutral particles can pass between the orbital electrons of atoms more readily than can charged particles such as alpha particles, beta particles, or the secondary electrons dislodged by x-rays or gamma rays. The neutrons thus have fundament-

rays upon rats and mice in order to know what precautions might be necessary for the protection of the men employed in the laboratory where the cyclotron was in operation

The author's brother, Dr. John H Lawrence, carried out the original experiments which demonstrated that rats exposed to the neutron rays for only a few minutes died in the course of two or three days. In measuring intensity of the neutron rays a Victoreen condenser

NEUTRONS & X-RAYS ON 5 OBJECTS

| | RATIO |
|--|--------------------------|
| MAMMARY CARCINOMA X-RAY 3600 N NEUTRON 700 N | 5.1 |
| NORMAL MICE [LETHAL POWER] | 3.8 |
| DROSOPHILA EGGS \[\begin{pmatrix} X-RAY & 180 \\ NEUTRON & 87 \\ \begin{pmatrix} X-RAY & 180 \\ \text{NEUTRON} & \text{NEUTRON} & \text{NEUTRON} & \text{NEUTRON} \\ \text{NEUTRON} & NEUT | 2.1 [ZIRKLE & AEBERSOLD] |
| WHEAT SEEDLINGS - X-RAY 600 x7 NEUTRON 120 x | 5. " |
| FERN SPORES [X-RAY 52,000] NEUTRON 21,000] | 2.5 " |

Fig 29—Summary of comparative effects of x-rays and neutron rays on five biological objects, showing that the ratio of the doses of the two forms of radiation required to reproduce the same biological action in the several instances varies from 2 1 to 5 1. These results show that neutrons have a selective action on biological substances which in general is different from that of x-rays (Courtesy, Radiology, Sept., 1937)

ally a different effect upon matter than haxe x-rays or gamma rays. Dr. Lawrence was interested in comparing the lethal effect of neutron rays upon living cells with the effect of x-rays upon similar cells. Further he was interested in finding out if there might be a different effect upon cancer cells than upon normal tissue cells. If he could demonstrate that neutron rays killed cancer cells and at the same time did not kill normal tissue cells then the neutron rays might have clinical application in treating cancer patients. Experiments were made to determine the lethal effects of the neutron

"r" meter was used The same instrument was used to measure the intensity of the x-rays employed in comparative experiments. The specimens of mouse mammary carcinoma, mice, Drosophila eggs, wheat seedlings, and fern spores which served as the biological test materials were placed in a compartment in a wooden block at a distance of seven centimeters from the beryllium target of the cyclotron

This demonstration that neutrons differ from x-rays, in their effect upon normal mice, cancer cells, eggs, seedlings and spores has encouraged Dr Lawrence

to build a larger cyclotron in which the output of neutron rays might be great enough to use in attempts to cure cases of cancer in human patients

SKIN DISEASES

X-ray therapy is considered by A M. H Gray to be one of the most valuable means of treating skin diseases, but it has its dangers as well as its advantages A single small dose of x-rays applied to delicate normal skin, as for example, on the forearm, produces no visible effect If this is repeated several times, or if the dose of a single treatment be raised to a certain threshold value, there may appear a redness after about a week This may last three or four weeks and then be followed by pigmentation lasting for several weeks more When larger doses are applied, the erythema appears earlier and lasts a longer time larger the dosage, the more likely are additional effects, such as edema, vesication, ulceration and pain Even after healing has occurred, there may be an atrophic scar, devoid of hur and sweat glands, and disfigured by irregular patches of pigmentation and telangiectasis Even small doses repeated many times may cause this atrophy and scarring of the skin. It may take many years for these changes to develop A certain threshold dose of x-rays applied to the scalp may cause the hair to fall out in the treated area. If this epilation dose has not been exceeded, the hair will grow in again, so that in the course of a few months it will have entirely regrown If, however, this threshold epilation dose has been exceeded the hair may never grow in again But the treatment of hypertrichosis by x-rays is strongly condemned, because in order to remove the hair permanently such large doses are necessary that the skin cells must be

injured Telangiectatic scars are likely to result which cosmetically are far worse than the original hypertrichosis

Epilation by means of x-rays is a valuable help in the treatment of ringworm of the scalp. The x-rays do not kill the fungi of ringworm, but bring out the hairs so that the antiparasitic ointment will have a better chance to act. If epilation is attempted, for this purpose, it should be carried through to completion. A single epilation dose is given to each of five areas.

There are many skin diseases which respond favorably to x-ray treatment, or a combination of x-rays and other means, according to Gray Among these are eczema, eczematous occupational dermatitis, chrome eczema of the palms and soles with hyperkeratosis, lichenified eczemas of the flexures, psoriasis localized in small areas, lichen planus localized in small areas, acne vulgaris, folliculitis of the beard region, pruritus ani, pruritus vulvae, hyperhidrosis of axillae, hands and feet, mycosis fungoides, warts, keloids and malignant skin growths There are several conditions that do not respond to x-ray treatment as favorably as would be expected Among these conditions are lupus erythematosus, exfoliative dermatitis, pityriasis rubra pilaris, congenital tumors, vascular nevi, moles, linear nevi, ichthyosis, and hystrix

EPITHELIOMA OF THE LIP8

Radiation Treatment—The first case of epithelioma of the lip treated by irradiation at the Hospital of the University of Pennsylvania was in 1908. This case was far advanced and had metastases in the neck and did not respond to treatment. Since that time the technic has been improved by successive steps. Prior to 1927 only a few local lesions were treated with roentgen.

rays, the remainder were treated with radium In 1928 the filtration was increased to 15 or 2 mm of brass and doses of 400 to 2000 mg -hr were given It was then found that the radium was sufficient in itself to cure the average epithelioma of the lip In 1932 a few cases were treated with superficial roentgen therapy and the results were so good that a year later, the use of radium was The choice of roentgen discontinued rays in preference to radium was not due to any better curative value of one form of irradiation over the other, but to the fact that the roentgen dosage can be given in a shorter time, and can be applied more evenly and measured more accurately The treatment factors were 135 Ky, 5 ma, 30 cm, 7000 to 10,000 r, approximately two-thirds unfiltered and other third filtered through 1 mm aluminum Occasionally two or three portals were used giving 3600 to 7200 r to each In 1936 a Siemen's contact therapy machine was installed and the factors used were 50 Kv, 4 ma, 02 mm copper filter, 3 cm distance, 5000 to 10.000 r Results of this latest form of treatment can not be reported yet There are 285 cases of epithelioma of the lip in the series reported by the author The cure of the local lesion on the lip was found to be a relatively There were only ten simple matter local recurrences, only two of which occurred in the last ten years Recurrences are usually easy to cure but there is always the danger that metastases may develop, thereby making the prognosis much more gloomy Less than five per cent of the patients who developed metastasis were successfully cured If a patient has moderately advanced metastasis to the nodes of the neck when he first seeks treatment, the chance of cure is slight

The author has summarized his findings in the following rules:

- "1 A routine block dissection of the lymphatics of the neck for epithelioma of the lip is impractical in the absence of metastasis because:
- (a) A large number of patients with epithelioma of the lip never develop palpable nodes in the neck at any time
- (b) Most palpable nodes in these cases are benign
- (c) Very few patients develop metastasis after the local lesion on the lip is cured
- (d) An appreciable morbidity and mortality follows block dissection
- 2. Routine prophylactic irradiation to the neck is probably impractical in the absence of metastasis because:
- (a) A large number of patients with epithelioma of the lip never develop palpable nodes in the neck at any time
- (b) Most palpable nodes in these cases are benign
- (c) Very few patients develop metastasis after the local lesion on the lip is cured
- (d) Prophylactic irradiation, in amounts small enough to be practical, is probably not sufficient to cause the death of any cancer cells which may be present in the lymphatics. Such irradiation, however, may render the tissues of the neck less fertile for the growth of cancer metastases
- 3 Local discrete metastases which have not perforated the node capsule should receive 3000 to 5000 r external irradiation, preferably by highly filtered deep therapy. At the appropriate time they should then be removed surgically. Such discrete metastatic nodes should not be treated by external irradiation alone because they are radioresistant in most instances. An alternative here is to give external irradiation and then follow this by surgical exposure and implantation

of radon or radium needles The former plan, however, is the better of the two

- 4 Small fixed metastases should be exposed surgically and implanted with radon or radium needles after receiving 3000 to 5000 "r" external irradiation. No attempt should be made to remove them because of the difficulty in effecting a complete extirpation.
- 5 Extensive mass metastases should be given only palliative doses of external irradiation, since there is no known method of cure, and any drastic measures will probably kill the patient or at least make his condition worse. Such irradiation should be applied in daily small doses. Large doses tend to cause the center to breakdown and become necrotic, especially if there is a superimposed infection in the mass.

MALIGNANT LESIONS OF THE LIP

Radiation Therapy — Treatment of malignant lesions of the lip⁹ must depend upon their position, extent, whether ulcerated and infected, and most of all whether there is extension to the lymph glands of the neck. In the series of 160 cases reported by the author, 22 had palpable lymph nodes at the time of admission. It was uncommon to find palpable nodes within six months from the onset of the local lesion.

In determining the course of treatment the age of the patient was considered for it was found that younger patients required more drastic treatment to control malignancy than did older patients. In older patients with localized lesions on the lip, surgery was usually the method of choice. It eliminated the entire malignant condition and irradiation was then given to prevent recurrence and metastasis.

It is advisable to obtain a biopsy on all lesions of the lip. In cases where the lesion is small, the biopsy specimen may to advantage include the whole lesion. In most cases microscopic examination of sections will disclose squamous-cell epithelioma.

In all cases, whether surgery or irradiation, is employed, treatment begins with either radium or high voltage x-rays directed against the lymphatic system which drains from the lip lesion When x-rays are employed both sides of the neck are irradiated More intensive treatment is given if nodes are already demonstrable Fields 9 by 12 cm or 10 by 15 cm, sufficiently large to cover the whole neck area, are given a dosage of 150 to 200 r per day every second day A total dose of 850 to 3000 r is given each field, depending upon the extent of lymph node involvement The factors employed are 200 Kv, 4 to 5 ma, 05 mm copper plus 1 mm aluminum filter at 40 to 50 cm distance In some cases, with advanced lesions a modified Coutard method of x-ray therapy is employed Each side of the neck is given 3000 to 5000 r through 2 mm of copper filtration at a distance of 50 to 60 cm in the course of 30 days. As a result of such intensive therapy, marked skin reactions may appear and hospitalization may be required until the irradiation effect subsides

Where neck node dissection has been decided upon, preoperative x-ray therapy is administered to both sides of the neck. The dose given is 900 r per area over a period of six days, 150 r being administered to each side of the neck each day. Operation may be carried out within three weeks following x-ray therapy.

Kaplan gives in detail the method of using radium instead of x-rays for the external irradiation of the lymphatic

dramage areas of the neck The method must depend upon the amount of radium available At Bellevue Hospital, New York, the five-gram pack is often used. In other cases a special mould may be made to fit the neck like a collar and in this mold are placed tubes of radium or radon spaced at proper intervals to radiate the desired glandular areas In some cases, in which definite lymph nodes are present, blocks of wax, wood or rubber sponge are fitted to each side of the neck and held in place with a head bandage Ten tubes of radium, ten milligrams each have been fitted into the blocks in suitable positions to radiate the affected glands

Following irradiation of the lymph node areas of the neck the local lesion on the lip is treated by means of surgery, radium, x-rays or a combination of these During the course of the local treatment the patient is hospitalized

In cases in which the lip lesion is to be treated by radium, a mould of wax or rubber is prepared to completely inclose the lip and to hold it downward and forward away from the teeth Usually four or five tubes of radium of ten milligrams each are enclosed in the mold in such positions as to irradiate the lesion from the front, above and below

Lead plates are incorporated into the mould to shield the tissues which should not be irradiated. The mould is held in place by adhesive plaster or by bands of tape around and over the head. The mould is removed at meal times and is cleansed and replaced immediately afterwards. The patient suffers little, if any, discomfort from this method of treatment even though it lasts from two to six days. Tube filtration consists of 1 or 2 mm of platinum or its equivalent in lead. The total dosage is from 1500 to 3500 milligram hours. In a typical case used for illustration the wax mold was

0.5 cm thick, contained four radium tubes of ten milligrams each and was held in place 72 hours, making the dosage 2880 milligram hours

In cases in which the lip lesion is to be treated by x-rays, a protective lead shield is prepared. It is cut out to fit the lesion exactly so as to allow the rays to strike only the lesion. As treatment progresses and the lesion becomes smaller other protective shields are prepared with smaller cut out portals.

Low voltage unfiltered x-rays are used with the following factors, 100 to 150 Kv, 4 to 5 ma. no filter, distance 30 to 40 cm field, just sufficient to include the involved area. The dose given is from four to ten erythemas over a period of 21 days, four or five skin erythema doses being administered each day to the involved area. Following treatment, the lesion is handled as a second degree burn. Wet dressings are applied for several days and then a bland ointment dressing is used until the lesion is healed.

When recurrences appear they are usually eradicated with surgery They may be irradiated by radium in packs or moulds or by interstitial implantation of radium needles or radon seeds

In cases in which lymph nodes are relatively resistant to external irradiation, and persist after such treatment, they are usually removed surgically. In some cases they may be given interstitial radium therapy by inserting radon gold seeds of from 0.2 to 1 millicurie each into the palpable nodes. The number of seeds employed varies with the size of the nodes being treated. A dose of from 100 to 300 millicurie-hours per cubic centimeter is used.

The author's results of irradiation in cancer of the lip, based on the study of the 160 cases reported, compare favorably with those following surgery. Irradiation has the added advantages of no

immediate operative mortality and mutilating scars are very much less likely to occur.

NEGLECTED AND RECUR-RENT BASAL CELL EPITHELIOMAS OF THE FACE

Meyer¹⁰ makes a strong plea for adequate treatment of basal cell epithelioma of the face. The initial treatment is the most important for if there is a recurrence the epithelioma is likely to grow more wildly than before the treatment

be eradicated by the highly trained expert who is willing to give heavy enough dosage to destroy the underlying cartilage or bone. Similarly, if a surgeon excises the cancer and does not take along the underlying cartilage or bone a recurrence will take place and necessitates a later, much more extensive and mutilating operation.

Physicians using x-ray and radium must learn to recognize those lesions which are rayresistant. If irradiation given in proper doses does not cure



Fig 30, left—Recurrent epithelioma of cheek following curettement Fig 31—Appearance of cheek following use of escharotic (Courtesy, Surgery, Gynecology and Obstetrics, March, 1937)

Basal cell epitheliomas of the face are seen early, can be diagnosed early and do not metastasize to distant parts of the If treated radically and early, a cure should be effected They may be destroyed by properly dosed and efficiently given x-ray or radium, galvanocautery, or electrocoagulation or may be removed by surgical excision method makes no difference just so long as the lesson is thoroughly and completely destroyed, or removed It is much easier to destroy or remove a basal cell epithelioma if it has soft parts underlying it than if it has cartilage or bone immediately underlying it Even in this more serious location the epithelioma may

a lesion early then irradiation will surely not cure it later and the case should be referred to the highly trained cancer surgeon Similarly, if the average surgeon has operated on a basal cell cancer and a recurrence appears he should likewise not attempt a second small operation but should refer the patient to a cancer surgeon specialist for a radical Meyer reports four cases operation which illustrate these points Early attempts had been made to cure basal cell epitheliomas of the face. After recurrences very extensive operations were required to remove the cancer cells from underlying bone and cartilage The defects in the face were repaired by reconstructive surgery Meyer presents photographs and details regarding the operations to make his points emphatic

MALIGNANT TUMORS OF THE ORAL CAVITY AND PHARYNX¹¹

Radiological Treatment—At Radiumhemmet, Stockholm, malignant tumors of the oral cavity are usually treated with radium, rarely with x-rays For teleradium treatment, there are two large

to compute the depth dose reaching a deep seated tumor when the radiation is applied by cross-firing through several portals.

In interstitial treatment radium needles containing ten milligrams for each centimeter of length are implanted. The needles have filtration equivalent to 05 millimeter of platinum. They are left in position in the tissues for three or four hours.

In surface applications radium tubes containing 25 milligrams, with filtration



Fig 32, left—Pedicle flap healed in place, defect on forehead, and under surface of pedicle closed with Thiersch skin graft are shown in this illustration
Fig 33—Flap healed in place, pedicle returned to forehead Two months after operation

(Courtesy, Surgery, Gynecology and Obstetrics, March, 1937)

bombs, one containing three grams and the other five grams. The filter consists of five millimeters of lead so only the very hard gamma rays are used in the treatment Special condenser chambers have been designed so that the measurement of intensity of radiation can be done with a high degree of accuracy These condenser chambers are small and can be applied to the surface of the tumor. or can be inserted into the tissue of the tumor so that the intensity applied to any point can be measured Depth dose charts prepared from measurements obtained in this way are shown By using these depth dose charts it is possible

equivalent to 0.5 millimeters of platinum, are employed. For application to the tonsil region a special instrument has been devised by Berven.

The treatment is begun with teleradium therapy. After the reaction has subsided any small tumor remnants are treated by radium implantation, surface application, electrocoagulation or a combination of these methods. Finally, if any remnants remain, they are removed surgically. The technic of treatment is described by Berven in the following way.

"In the introductory teleradium treatment we try to radiate the primary

tumor and the lymph node metastases, simultaneously as if they formed one continuous tumor and we use as far as possible a homogeneous dose which is attained by multiple fields and cross-fire radiation. The daily dose and the total dose must be carefully individualized with special attention to a number of factors all of which influence tumor healing.

- 1 The patient's general condition, his age, any previous treatment and any luetic infection
- 2 (a) The clinical character of the tumor, its size and any disintegration or secondary infection
 - (b) The extent of the tumor
 - (c) Infiltration of neighboring organs
 - (d) The presence of metastases
 - (e) The character of the tumor
 - 3 The histology of the tumor
- 4 The character and intensity of the treatment reaction produced in the mucous membrane and skin

"As a rule we try to attain in the tumor surface and the surrounding mucous membrane the reaction which Coutard has described, under the term epithelitis and in the skin a reaction which he calls an epidermitis The epithelitis has the appearance of a thin, vellowish, fibrinous, confluent membrane This membrane formation does not seem, however, to be pathognomonic for radiation but can be produced as an inflammatory reaction in the mucous membrane and underlying tissues by agents of very varying types Coutard at first considered that the epithelitis was an indication of the epithelicidal dose, i e, the dose which effectively destroys the epithelial cells of the mucous membrane, and should therefore produce destruction of the usually more radiosensitive tumor cells It would seem. however, as if this conception has not sufficient biological basis, since, for instance, a number of tumors of the oral cavity can be made to disappear without an epithelitic reaction developing in the surrounding mucous membrane and since tumor healing is influenced by many factors other than the radiosensitivity of the tumor cells The intensity of the epithelitis, however, seems to be in direct proportion to the size of the dose and the reaction would therefore still seem practical as a biological indication of the dose The epithelitis usually appears 14 to 15 days after the beginning of treatment According to the size of the dose it may be an epidermitis sicca. exsudativa or necrotica The usual dosage gives an epidermitis sicca or a moderate epidermitis exsudativa which is as a rule healed within two to three months after the conclusion of the treatment"

"One of the main prerequisites for a favorable course of the healing process is the infliction of the gravest possible damage upon the tumor cells with at the same time the least possible injury to the surrounding tissues through which the resorption, regeneration and nutri-The intion are going to take place flammatory reactive phenomena in the surrounding tissues are in direct proportion to the size of dose, are caused by the injury of cells in these tissues and must therefore be as nuld as possi-By suitably adjusted protraction and fractionation (relatively small doses of low intensity repeated over a long period of time) these reactions in the neighboring tissues can be kept relatively In order to obtain a favorable result both the epithelitis and the epidermitis must be kept within limits which do not cause the patient any serious inconvenience"

"Of 457 oral cavity cases treated, 114 (25 per cent) lived, free from symp-

toms for five years or more Of 39 cases of carcinoma or lymphepithehoma of the tonsils treated, 16 (41 per cent) lived, free from symptoms, for five years or more Of 49 cases of sarcoma of the tonsils treated, 17 (35 per cent) lived, free from symptoms, for five years or more "

Berven has drawn very important conclusions and gives us the benefit of his many years of experience in the following words

"Radiological treatment of malignant tumors entails the fulfilment of certain conditions in order that favorable permanent results may be obtained

"One of the most important prerequisites for successful therapy is a great number of cases without which it is impossible to acquire thorough clinical The variable clinical picexperience ture in malignant tumors means that every case presents a new problem and therefore requires individual treatment The evaluation of the local and general reactions accompanying the treatment likewise necessitates very wide experience The physician must therefore have access to all facilities for detailed clinical study as well as a modernly equipped roentgen department and a large quantity of radium allowing of all types of application

"Also essential is intimate co-operation with a radiopathologist who has specialized in the diagnosis and classification of tumors and the study of postradiation healing processes. The science of pathology is at present facing a period of rapid development and a revision of old conceptions is necessary in view of the daily findings in connection with the radiation of malignant tumors

"The dosage problem which is met with in the treatment of every patient, the development of new methods of treatment, the daily control of the technical details, the protective arrangements for the personnel and patients all require a well equipped and modern physics department directed by physicists who have devoted special study to radiophysics which has now reached such a stage of development that it is impossible for a physician to be acquainted with all the different details

"Careful supervision of the patient and a thorough follow-up after recovery are of the greatest importance not only for the attainment of a good result but also for the procuring of correct and comparable statistics. This task can only be fulfilled, if the clinic has at its disposal a department provided with a sufficiently large staff to control the follow-up and statistics."

CANCER OF THE BREAST

Conservative Treatment-In an address delivered to the American Surgical Association, the well known British surgeon, Geoffrey Keynes,12 stated that the treatment of cancer in all parts of the body has been disappointing but the treatment of cancer of the breast has perhaps been less disappointing than in most other positions. Surgeons who have followed up their patients, upon whom the Halsted radical removal of the breast has been performed, are indeed gravely dissatisfied with their results In order to decrease the mortality from cancer and to avoid the mutilation incidental to the radical removal of the breast. Keynes cautiously investigated the possibility of treatment by interstitial radium alone The first work was done in 1922, following a suggestion made by Professor George Glass During the first two years only patients with recurrent disease after operation were treated with radium. In nearly every patient the recurrence was made to disappear Encouraged by these

successes the radium treatments were tried on cases of inoperable or advanced cancer of the breast. After 50 such cases had been treated the results appeared to be quite remarkable and though the majority of patients died from metastases, many of the 50 patients lived for periods of eight years without external signs of the disease. Six of them are still alive

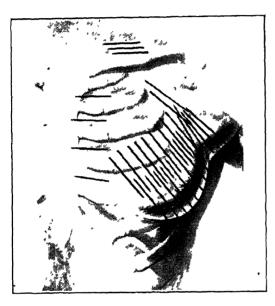


Fig 34—The radium has always been applied interstitially in the form of needles, the general principle being illustrated in this figure (Courtesy, British Medical Journal, Oct 2, 1937)

nearly ten years after treatment and five of these six, that is ten per cent of the whole, are without any sign of the disease

The results in these 50 cases caused Keynes to feel justified in trying the interstitial implantation of radium needles in the treatment of early cases of cancer of the breast. From that time up to the present time he has systematically used either radium by itself or in combination with very conservative surgery. The radium has always been applied interstitially in the form of needles, the general principle being illustrated in Fig. 34. The whole breast area.

is treated with long needles, such containing 3 mg radium element, placed in parallel series from each side and overlapping in the center. The axilla is irradiated with from four to seven needles, two of which can be introduced into the apex of the axilla through the pectoral muscles.

Care is taken to avoid placing a needle in too close proximity to the neurovascular bundle. Three shorter needles are introduced into the area above the clavicle, and, lastly, one of the shorter needles is placed in each of the upper three or four intercostal spaces Recently Keynes has been doubtful about the necessity for intercostal irradiation and has omitted them in most patients In his experience recurrences in intercostal spaces are exceedingly uncom-The radium needles are usually left in position for seven days Surgical operation, if employed at all, has preceded irradiation, and has been done with the electrical knife No dissection of the axilla has ever been carried out. though occasionally an infected gland close to the axillary tail of the breast has been removed

The patients were carefully observed, and in due course a certain number of failures were noted, as evidenced by incomplete disappearance of the primary tumor or by the appearance of recurrent nodules in the breast or in the skin Some of these residual tumors were removed and examined histologically nine months or more after the irradiation In 50 per cent no demonstrable cancer tissue remained but the whole mass was made up of fibrous tissue In the other 50 per cent there was evidence of active This finding caused cancer tissue Keynes to consider the whole subject carefully in an attempt to discover the cause of these failures to destroy all the cancer cells One cause might be

| Τ. | ABI | .F. | 3 |
|----|-----|-----|---|
| | | | |

| | Group | Number | Net Survival | UCH Survival |
|---------------|-------------|----------------|-------------------------|----------------|
| At 3 years | 1 2 3 | 85 91 74 | 83 5% 51 2% 31 4% | 79 2% 52 3% |
| At 5 years | 1 2 3 | 75 66 60 | 71 4% 29 3% 23 6% | 69 1% 30.5% |

that some types of cancer cells might be more resistant than others to the gamma rays A more probable cause appeared to be that due to the physical limitations of radium needles, in that the penetrating powers of gamma rays are limited Many of the tumors were too thick and bulky for the gamma rays to penetrate them effectively from below, so that the cancer cells in the center or at the surface did not receive a lethal dose As practical difficulties stood in the way of increasing the dosage of radium it was decided to reduce the size of the tumor mass by operative procedures, before irradiation As Keynes has stated this so concisely, his own words are quoted

"I therefore decided to remove more frequently either the tumor or the breast before irradiation, according to circumstances Sometimes in the earliest stages of the disease it was desirable to remove the tumor in order to establish the diagnosis Whenever an operation was done it was as conservative as circumstances would allow, and never was it allowed to extend to removal of the pectoral muscles or dissection of the axilla the majority of patients, therefore, the amount of mutilation was negligible, and for some, radium was still alone employed, without any operation at all This procedure could only be justified if it was clear that the effect of radium on the axillary lymph nodes was good It may be stated at once that close observation of the patients over many years has shown that the results in the axilla have been uniformly good. Large axillary nodes have been made to disappear almost with certainty, and they have not recurred. If the axilla did not contain palpable nodes none have developed afterwards. The facts have crystallized the procedure at the present time as follows.

- 1 Local removal of tumor if it is large or the diagnosis is uncertain, followed by radium.
- 2 Local removal of the breast if the tumor is very bulky, followed by radium
 - 3 Never dissect the axilla
- 4 Radium by itself may be used (a) If the tumor is of moderate size and the diagnosis certain on clinical grounds, (b) if the patient refuses operation. No patients have been treated without histological proof of the disease unless the diagnosis was quite plain from the clinical signs

"If the disease has extended to the supraclavicular nodes when the patient is first seen, this has usually been found to be accompanied by disease within the thorax, so that the patient will often be unsuitable for treatment by radium, which like surgical operation is essentially a local form of treatment. Apart from the obvious necessity of sometimes rejecting those who showed evidence of metastases in the viscera or skeleton, there has been no selection of patients"

Statistical Results — The patients have been divided into three groups

Group I—Disease apparently confined to the breast

Group II—Disease apparently confined to the breast and axilla

Group III—Disease advanced or inoperable

The figures have been compiled by a competent statistician. Patients treated in the last three years have not been included so the number available for statistical examination is 250. The numbers in the three groups and their net survival percentages after three years and five years are shown in Table 3.

Allowance has been made in the third column for patients who died of intercurrent disease and the figures therefore give the net survival rates. In the fourth column are given the survival rates obtained as the result of an investigation carried out by W. H. Graham Jessop (1936) at University College Hospital This was the nearest approximation available to a comparable series of a similar number of patients treated by surgery alone.

It is indeed significant that Keynes obtained approximately the same percentages of survivals three and five years after radium treatment as were obtained by good surgeons by radical operative treatment

These good results have led Keynes to question some of the fundamental theories upon which the radical operation was based. He maintains that if the axillary lymph nodes are extensively infected, dissection of the axilla may be harmful, and that if they do not appear to be infected, it is unnecessary, provided that radical irradiation is carried out in every patient. Keynes has difficulty in accepting the theory of lymphatic permeation by cancer cells. He cites the anatomical investigations carried out at St. Bartholomew's and University College Hospitals by J. H. Gray under the

inspiration of Professor H H Woollard The course of the lymphatics has been demonstrated by injecting thorotrast and barium This new work is more accurate than any which had been done previously and demonstrates the absence of lymphatic plexuses in the deep fascial layers The lymphatic system of the breast lies in the gland and on its surface, the main lymphatic trunks passing around the fold of the axilla to the axillary nodes No evidence whatever was found to support the theory of centrifugal permeation On the other hand normal lymphatic channels were found connecting a carcinoma with infected nodes, the only possible inference being that carcinoma cells pass to the nodes as emboli, usually without forming intermediate points The supposed permeated of growth channels have been shown to be generally infiltration in planes of tissue cleavage, or sometimes to be growth in a venule It follows, therefore, that widespread operations, based upon the permeation theory of lymphatics in fascial planes have no real justification. Keynes presents his conclusions in the following

"The foregoing account of a clinical investigation, which has now extended over 14 years, seems to me to show that the treatment of carcinoma of the breast may justifiably be made much more conservative than it usually is, provided that the necessary facilities for irradiation are available Statistics appear to demonstrate that a definite improvement can be obtained in the most favorable group of patients by judicious use of interstitial radium alone, or of radium combined with very conservative The rapid improvement in x-ray technic now taking place suggests that x-rays may perhaps be used as an alternative to radium according to cir-The treatment here advocumstances

cated is, however, conservative rather than purely radiological and details of the technic will no doubt undergo further modification. The general trend of surgery in the treatment of cancer is away from the very extensive operations formerly in vogue, and I believe that this may be found to be true of the future treatment of cancer of the breast. My own results with conservative methods encourage me to proceed in that belief."

The therapy of cancer of the breast has recently been reported in statistics from several well known hospitals Combined operation and irradiation is the method of treatment advocated by the majority of radiologists and postulates thorough radical mastectomy followed by irradiation adequate to destroy all cancer cells in the bed of the tumor and sur-Many radiologists rounding tissues confine their postoperative irradiation to the field of operation and axillary and supraclavicular regions Other radiologists give prophylactic irradiation to the lungs, mediastinum and vertebral column A Gunsett follows radical mastectomy by surface mould radium to the axilla, radium needle implantation in the internal mammary lymph drainage region, and x-rays by a protracted divided dosage technic to the tumor bed, supraclavicular fossa, thorax and spinal column

Different technic must be used in treating a primary carcinoma of the breast, a recurrence, or an advanced metastatic disease, according to Pfahler and Vastine. The technic must be varied with the stage, extent and type of the disease. In advanced cases repeated examinations must be made of the chest, the mediastinum and the bones for metastasis. When any suspicious areas are found, they must be carefully irradiated. The sooner recurrences and metastases are discovered, the more hope there

is of combating them. It is recommended that every patient with carcinoma of the breast be under observation for many years and be carefully examined at stated intervals

Preoperative Irradiation—A series of 81 cases of operable cancer of the breast is reported by F E. Adair and F W Stewart¹³ in which operation was delayed for several months in order to give irradiation previous to surgery The four-gram radium pack was used in 39 cases and high voltage (200 Kv) x-rays in 42 cases Breast and axilla were irradiated through five portals with the radium pack

Three to four months after this treatment radical amputation of the breast was done and the tissues were carefully examined In 11 (28 per cent) of the 39 cases no trace of cancer tissue could In 46 per cent there were be found changes produced by profound radium in the breast tumors In cases with axillary node involvement radium had produced profound changes in the nodes in only 195 per cent Because this indicated inadequate treatment a new method was devised long forceps was introduced behind the pectoralis muscles and brought out near the sterno-clavicular joint. The forceps was used to draw in a catheter containing six tubes of radon in tandem this means three to seven skin erythema doses, 3 mm from the radon were delivered It is yet too early to draw conclusions regarding this interstitial treatment

In the 42 cases treated by the highvoltage roentgen rays complete microscopic disappearance of the tumor occurred in seven (16.5 per cent) of the cases. The dosage consisted of 1200 to 1800 r to each of six portals

The authors conclude that pre-operative irradiation will definitely increase

the incidence of five-year cures and should be employed in all cases of cancer of the breast, in pregnant women, in cases with extensive axillary involvement, and the cases of young women

CANCER OF THE KIDNEY

In discussing the immediate effect of preoperative radiation in cortical tumors of the kidney, G C Prather and H F Friedman¹⁴ state that patients with renal cortex tumors have an average life of two to three and one-half years The mortality rate following nephrectomy is from 15 to 30 per cent depending upon whether the surgeons are cautious or daring The mere size of the tumor is one factor which makes surgery so difficult Preoperative x-ray treatment has reduced the size of some of these renal cortical tumors in a spectacular manner according to Waters, Bothe and Wharton X-rays were found to be especially effective in reducing the size of those tumors which were made up of embryonal cells

Waters, Lewis and Frontz reported a series of 15 cases showing 93 per cent radiosensitivity and Wharton reported two Grawitz hypernephromas and two Wilms' embryomas which decreased in size almost miraculously

Prather and Friedman emphasize the fact that spectacular reduction in size does not prove that a tumor has been cured. Bothe reported three cases, in children, in which tumors decreased in size to such an extent that the parents hoped that cures had been effected and would not permit surgery. Two of the children were dead within a year

Prather and Friedman were successful in shrinking one Wilms' tumor and two hypernephromas. In the second case of hypernephroma, a total dosage of 9000 r was given to the tumor mass through

three fields of 180 sq cm each The factors used were 200 Kv pulsating, 4 ma. 50 cm tube distance, filtration 2 mm. copper plus 1 mm aluminum, effective wave length 0 12 Å units, quantity 3 5 r per minute, daily dose 200 r to each of two fields morning and afternoon. The mass just before operation was about one-third of its original size

CANCER OF THE URINARY BLADDER

In an evaluation of surgery and irradiation in the treatment of this disease J R Andrews and C A W Uhle¹⁵ report their results following surgery alone, irradiation alone and the combination of surgery plus irradiation. The best results were obtained in the latter group in which 6 out of 27 patients treated by surgery plus x-rays lived five years, a survival rate of 22 per cent. Of the 15 patients treated by surgery alone only one lived five years, a survival rate of seven per cent.

Andrews and Uhle submit the following conclusions regarding the essentials for the optimum treatment of cases of carcinoma of the bladder

- 1 Cystoscopy should be correlated with pneumocystography or contrast cystography
- 2 A biopsy specimen should be obtained if possible
- 3 All patients in whom a diagnosis of carcinoma of the bladder has been made should first have a course of irradiation
- 4 After a sufficient time interval has elapsed to allow the normal tissues to recover from the radiation effects, but before the neoplasm has resumed active growth, radical surgery should be employed. This time interval is about six weeks. We believe that in cases in which the lesion is anything more than a small

pedunculated carcinoma nothing short of an open operation can be adequate. If facilities are available, radon seeds, gold filtered and of small radon content, should be implanted

- 5 The course of external roentgen irradiation should be repeated after convalescence
- 6 External irradiation, in patients who are inoperable, frequently proves of great palliative value in controlling bladder distress and hemorrhage
- 7 An efficient follow-up system is indispensable

TUMOR OF THE TESTIS 16

Value of Preoperative Irradiation

— The early method of treatment of tumor of the testis, by orchidectomy alone, was disappointing and showed less than ten per cent of cures Radical orchidectomy, with the removal of the entire lymph drainage area gave somewhat better results, with 19 per cent of cures

A great aid in the diagnosis of testicular tumors followed Zondek's demonstration, in 1929, of the presence of a gonadotrophic hormone in the urine of a man suffering from teratoma of the testis A qualitative and quantitative test has been developed so that now the number of mouse units of Prolan A in the urine may be determined. This can be applied as an index of the type of tumor and its probable degree of radiosensitivity. After proper irradiation of a testicular tumor, or its metastases, a prompt drop occurring in the number of mouse units of Prolan A excreted in the urine, is evidence of the sensitivity of the tumor The rapidity and extent of the decrease in Prolan A are excellent indices upon which to base the prognosis and Bothe have postulated the following in guiding their surgery

- 1. The younger the cell, the greater its roentgen ray sensitivity
- 2. The younger the dominant cell type, the more frequent and the earlier the metastases
- 3 In the face of existent metastases, irradiation should, of course, precede the orchidectomy
- 4 If this last be true in gross visible metastases, it should be even more essential if metastatic involvement is just beginning

Based on these postulations, during the past three years the authors have adopted the following procedure

- 1 Have a Wassermann and a Prolan A determination
- 2 Begin immediately the administration of deep roentgen therapy.
- 3 Perform an orchidectomy about five weeks after the last roentgen ray treatment

The deep x-ray therapy is given first in the periphery, converging toward the focus of the disease In testicular tumor irradiation the lymphatic channels are included from the chin to the tuber ischii anteriorly and posteriorly, it being hoped, thereby, to destroy metastatic foci, to create a field resistant to malignant cell implantation, and, finally to administer daily to the immediate lymph drainage radicals and the local tumor, a small, protracted dose up to the limit of skin tolerance The general resistance of the patient must be kept in mind and can be checked by blood counts done every two weeks. The authors have classified the tumors of the testis in three groups according to their sensitivity to irradiation Photomicrographs are presented to show the histological effects produced by roentgen rays in tumors of these three groups In general, these show that irradiation of testicular tumors has a definite destructive effect upon the immature embryonal cells, but little or no effect

upon the differentiated types. These observations are in keeping with the laws governing cellular radiosensitivity

In view of these findings, it is evident that, regardless of the degree of clinical improvement irradiation does not entirely destroy the neoplasm. In that class in which there were occasional viable cells remaining which appeared to have the power of regeneration, surgical removal of the tumor was indicated. The proper time for this operation was in the fifth or sixth week, when the maximum regression following irradiation was obtained.

Randall and Bothe predict that their newer technic of preoperative irradiation followed by orchidectomy will give far better results, with a much higher percentage of cures of tumors of the testis

In discussing the paper of Randall and Bothe, Frank E Adair, of the Memorial Hospital in New York, stated that teratoma of the testis is one of the most malignant of all human tumors. The classification which is used at Memorial Hospital is as follows.

- 1 The adult type those possessing cartilage, lung tissue, etc. The incidence is about ten per cent.
- 2 The seminoma—the large cell type Incidence, 16 per cent
- 3 The embryonal carcinoma with the lymphoid stroma, very radiosensitive Incidence, 40 per cent
- 4 Embryonal adenocarcinoma Incidence, 33 per cent
- 5 Chorioepithelioma Incidence, one per cent

Testing the urine for Prolan A has proved to be one of the most important diagnostic aids. If more than 100 mouse units per cc are found, the presence of teratoma of the testis is at once suspected. The quantitative findings may even help in establishing the histopathology of the tumor. The Prolan A test

becomes a valuable aid in the periodic follow-up of the case. It is an easy matter to test the patient's urine at intervals after treatment. The presence of excessive amounts of Prolan A is a sign of recurrence or metastasis. This test is far more delicate and reliable than any clinical or roentgenologic examination.

The treatment used at the Memorial Hospital at present consists in preliminary radiation of the testis and surrounding area, including the lower quadrants of the abdomen, the suprapubic area and the inguinal lymph nodes Approximately six weeks later orchidectomy is performed. Following the operation, the patient is irradiated by the divided dose technic, from the level of the diaphragin down to the trochanters both anteriorly and posteriorly.

Adair thinks that this combination of preoperative irradiation, and postoperative irradiation by the divided dose technic will give better results than those reported from his hospital in 1928 when 29.2 per cent were found to be free of disease five years after irradiation. In fact, Ferguson of Memorial Hospital, utilizing this newer technic, has obtained freedom from disease in a three-year period, of 52.6 per cent.

PROSTATIC CARCINOMA

Barringer¹⁷ presents the evidence submitted by various urologists regarding the origin of *carcinoma* of the prostate, as there seems to be a lack of agreement among them. From this diverse evidence he deduces the following. "Carcinoma in the great majority of cases originates in the posterior lobe. In most cases there is one focus of origin. If the carcinoma is of sufficient size to be diagnosed clinically, the posterior lobe is almost certain to be involved.

"The lateral and subcervical lobes may be involved secondarily or more rarely they may never be involved

"There may be multiple foci of origin of the carcinoma, that is, in the posterior, lateral, subcervical or anterior lobes"

Diagnosis by Aspiration Biopsy— The proper use of aspiration biopsy in early suspected cases of prostatic carcinoma is an important factor in solving the question of control of these cases Satisfactory specimens for examination by the pathologist can be obtained by aspiration in about 80 per cent of cases

Operative Treatment—In the hands of Young, who originated the radical surgical removal of prostatic carcinoma, there have been some brilliant five year cures No other surgeon has had as favorable results in general. The operation is applicable to only a comparative small percentage of cases so the vast majority must be treated by irradiation.

Irradiation - The best method of deep x-ray therapy has been developed by Coutard He gives daily treatments to four or five portals with 200 Kv and 300 r to each portal This is continued until 1500 or 1800 r have been given to each portal Even this is not heavy enough irradiation and must be augmented by some form of irradiation within the prostate itself The implantation of radon seeds and of radium needles is a difficult procedure if the whole prostate is to be irradiated adequately The implantations must be made by both the suprapubic and permeal approaches One treatment will usually not suffice and implantation must be repeated at intervals until the prostate is sclerosed

CARCINOMA OF THE CERVIX UTERI

Radium vs. Wertheim's Hysterectomy—Shaw, 18 of Manchester, one of

the best English gynecologists, has had many years of experience with Wertheim's hysterectomy. In a series of 154 cases of carcinoma of the cervix treated by him by radical operative procedure, 38 per cent were alive and well five years later. The operation still is serious and showed a mortality rate of 21 per cent in this series. Patients who survive are desperately ill for several days, suffer much pain and require many weeks for convalescence.

Shaw tried to improve his results by using radium instead of surgery His technic was modified somewhat from that used by Heyman in Stockholm Platinum containers, with wall thickness of 1 mm, holding 40 milligrams of radium were introduced into the uterine cavity Sixty milligrams of radium in 15 needles of four milligrams each with wall thickness of 05 mm of platinum were enclosed in three box applicators, with walls of silver 16 mm thick, and applied to the vaginal aspect of the cervix and vaginal fornices Each patient was given three treatments of 24 hours each with an interval of one week between the first and second treatments and an interval of three weeks between the second and third treatments The total dosage was 7200 milligram hours

In the first 94 cases treated with radium, Shaw observed that 41 per cent were alive and well after five years, which is very nearly the same survival rate as in his series following Wertheim's hysterectomy. The immediate mortality rate following radium was only 21 per cent or one tenth as great as the operative mortality.

Shaw quotes the report for 1935 published by the Marie Curie Hospital in London showing that in a series of 392 cases of carcinoma of the cervix treated by radium, 36 per cent were alive and well five years later. It is interesting

that this survival rate is so nearly the same as that in Shaw's own series. The following conclusions are given in the author's own words "After careful observation of these cases for over seven years, Professor Dougal and I have come to the definite conclusions that radium offers the best chance of cure as well as being the more humane method of treatment Therefore, strong advocates though we were of the operation, we have now abandoned it

"These figures, however, do not warrant any complacency A record of 40 per cent alive and well at the end of five years allows of hope but no self satisfaction. Eventually, the cause will be found and prevention or cure will follow, but until that object is achieved, we must use as best we can the imperfect weapons put into our hands."

In the discussion which followed Shaw's paper, Floyd E Keene, of Philadelphia, said in part

"I am in full accord with Dr Shaw's conclusions regarding the comparative value of the Wertheim operation and irradiation. My experience dates back 30 years to the early days of my apprenticeship with Di John G Clark when radical operation was at the height of its popularity. Its technical difficulties, high mortality and morbidity, and disheartening end-results remain a vivid Radium was introduced into memory our clinic by Dr Clark in 1913 For a time its use was limited to the advanced lesions, but as evidence of its value increased, its sphere was gradually widened until finally operation was discarded in its favor A hysterectomy for cervical cancer has not been performed in our clinic in the past 15 years.

"In these 20 odd years, our methods of application, dosage and filtration have been modified from time to time. For

the past four years, the dosage has ranged between 4800 and 6000 milligramhours with a filtration of one millimeter of platinum and two millimeters of rishber for the intrauterine radium and two millimeters of platinum with one centimeter of rubber in the form of the colpostat or capsules for the application to the vaginal fornices and cervix. Roentgen therapy has supplemented the radium in all cases with the exception of those with stage four lesions, in these. roentgen therapy alone is used, with radium application later when indicated Repetition of the treatment is not carried out at regular intervals, but only when conditions which warrant it arise Experience has taught us that the ultimate result is dependent upon what has been accomplished by the initial treatment, if this fails, not much can be expected from subsequent applications"

H C Pitts and G B Waterman¹⁹ give a report of 293 cases with five-year follow-up

Radium may be used in therapeutics in three ways

- 1 As a caustic agent to slough out a tumor Used in this way it will slough out normal tissues at the same time
- 2 As a selective destructive agent to kill tumor cells without destroying the normal tissue cells. Such a result is the aim of all modern treatment but is difficult to achieve especially in cases where the tumor cells are radioresistant.
- 3 As an *indirect agent*. The experimental work of Russ, Chambers and Scott strongly points to the production, during the destruction of cancer cells, of some factors resembling antibodies. These antibodies have the property of destroying metastases. If the destruction of the primary cancer cells is accomplished slowly they produce more antibodies than if the destruction takes

place rapidly This indicates that the more favorable method is to use small but long continued applications of radium rather than large doses applied for short periods

The authors have kept in mind this third method of using radium and have employed small units, heavy filtration and long periods of time

Radium may be applied in three ways

- 1. Surface Radiation—By means of packs, tubes and plaques against the surface of the cervix, vaginal vaults and the cervical canal
- 2 Interstitual Radiation—Insertion of seeds of radon or of radium needles into the tumor tissue itself
- 3 Distance Radiation or Teleradium—Employment of a pack containing a large quantity of radium (two to four grams) The authors have not employed this method of teleradium in any of the cases reported in this paper

Surface irradiation is the form of treatment for cancer of the cervix used in most European and American hospitals. There is wide variation in intensity as well as in the time factor but filtration is quite uniform at about the equivalent of two or three millimeters of lead. Four technics are given as illustrations

1 High Intensity-Short Time Interval—This method is practiced for instance at the Memorial Hospital in New York by Healy. He uses about 3000 millicurie-hours in the vagina, by means of a 1000 millicurie bomb for one hour in three directions, against the cervix and against each lateral formix. In addition he uses a tandem of two tubes (200 millicurie in lower segment and 100 millicurie above in cervico-uterine canal for ten hours). Total, 6000 millicurie-hours. External radiation by x-ray is used some weeks later.

- 2 Medium High Intensity-Longer Time Interval - Interrupted Treatment-This is the method at Radiumhemmet, Stockholm, and in most English hospitals Here the same total dose used by Healy is employed but divided into two or three fractions Each treatment consists of the application of about 40 milligrams in tubes in the uterus and 80 milligrams in the vagina in the standard boxes with an average time interval of about 20 hours (2400 milligram-hours per treatment) A second treatment is given one week after the first, and a third treatment is given two weeks after the second, and a fourth treatment is given after another two weeks In the later treatments a shorter duration may be employed so that the total application may be about 60 hours (7200 milligramhours)
- 3 Low Intensity-Long Time Interval—This is the method used by Regaud and Lacassagne at the Paris Institute Regaud was perhaps the first to advocate small, well distributed, heavily filtered units of radium for time intervals of five days

He removes the tubes, cleans them and replaces them once every 24 hours. He uses two tubes of 13.3 milligrams and one tube of 6.66 milligrams radium element in the uterus and the same size tubes in the vagina. The three tubes used in the uterus have one millimeter of platinum filtration while the three tubes used in the vagina have 1.5 millimeters of platinum filtration. In the five days (120 hours), the total dosage is thus nearly 8000 milligram hours (3991 to the uterus and 3991 to the vagina).

Most American clinics use radium applicators with less filtration—one-half millimeter silver plus one or two millimeters brass. The total dosage of 3000 to 5000 milligram-hours is spread out in two or three treatments.

The authors have reported their results in treatment during two periods of five years each. In the first period, 1921 to 1925 inclusive, there were 120 cases. In the second period, 1926 to 1930 inclusive, there were 173 cases.

In the first period the plan was to deliver a total dose of 3000 to 4000 milligram-hours in two or three treatments two or three weeks apart The technic was to place two tubes of 50 milligrams each in tandem in the cervical canal The filtration in this case was 05 mm silver, 1 mm of brass plus 1 or 2 mm of rubber Then a pack was placed against the cervix This pack was made up with one tube of 50 milligrams and two tubes of 25 milligrams with filtration of 0.5 mm silver plus 1 mm of The authors also had available ten needles containing five milligrams each These were encased in steel alloy In some patients they were implanted into and around the cervix while in the treatment of other patients the needles were included in the pack

In 1926 the authors received the following additional radium enclosed in platinum containers. The needles were long and they were thus adapted to the technic of small dosage used over an extended time spaced one to two centimeters apart In the cervical canal was placed the 20 milligram tube, usually held in place by a strand of silkworm gut. In some cases the tandem of two 50 milligram tubes in silver and brass containers was used instead of the 20 milligrams in the platinum container.

In 1926, 1927 and 1928 the radium was left in place 72 to 96 hours when all platinum containers were used. In 1929 and 1930 the radium was left in place 144 to 168 hours. The authors believe that this increased time of application has improved their results.

The authors have explained in detail the results which are given in the tables 4 to 7 inclusive. It is indeed interesting to compare their five-year survival rates under the different methods of treatment. In the first five-year period, the gioss survival rate was 20 per cent. When much more extensive treatment (6000 to 10,000 milligram-hours) was given the survival rate increased to 26.3 per cent. As will be noted in Table 7 this is a higher survival rate than shown for any of the other world famous clinics listed.

Conclusions

The conclusions drawn by the authors are as follows

| | Active Length | Wall |
|---|--|--|
| 2 × 20 mgm tubes 20 × 2 mgm needles 10 × 3 mgm needles 4 × 4 mgm needles | 36 to 40 mm 30 mm 45 mm 39 mm | 0 5 mm platinum 0 5 mm platinum 0 5 mm platinum 0 5 mm platinum |

The plan of the treatment was then changed Four of the three milligram needles were placed out in the tissue at the sides of the uterus, two needles at each side Then 12 to 16 of the two milligram needles were thrust into the tissue in front and behind the cervix and

"We believe that these figures show that interstitial radiation according to our technic, *i e*, low intensity long needles with 0.5 millimeters platinum filtration well distributed out in the paracervical and parametrial tissues, has a distinct value in the treatment of cervical cancer

RESULTS

TABLE 4—SURVIVALS BY CLINICAL STAGE—TOTAL 1921 TO 1930

| Stage | Total | 1 | 2 | 3 | 4 | 5 | Per Cent | Per Cent | Opera- bility | Died of Ca. in 6th year | Survival 6 yrs symptom free after 5 years | Per Cent |
|-------|-------|-----|-----|----|----|----|-------------|-------------|------------------|----------------------------|---|-------------|
| I | 14 | 14 | 13 | 13 | 13 | 13 | 92 8 | 1 | 1 | 2 | 11 | 78 5 |
| -II | 71 | 66 | 52 | 47 | 44 | 40 | 56 3 | 62 3 | 1 | 2 | 38 | 53 5 |
| III | 105 | 79 | 49 | 31 | 26 | 24 | 22 8 | | | 4 | 20 | 190 |
| IV | 103 | 19 | 7 | 3 | 3 | 2 | 19 | | | 0 | 2 | 19 |
| Total | 293 | 178 | 121 | 94 | 86 | 79 | 26 9 | | 29 0 | 8 | 71 | 24 2 |

(Courtesy, Surgery, Gynecology and Obstetrics, January, 1937)

Table 5—Survivals by Clinical Stage—Total 1921 to 1925—First Method—Brass Capsules, Steel Needles

| Stage | Total | 1 | 2 | 3 | 4 | 5 | Per Cent | Per Cent | Opera- bility | Died of Ca in 6th year | Symptom free after 5 years | Per Cent |
|-------|-------|----|----|----|----|----|-------------|-------------|------------------|---------------------------|-------------------------------|-------------|
| | 4 | 4 | 4 | 4 | 4 | 4 | 100 0 | 1 | | 0 | 4 | 100 0 |
| II | 19 | 18 | 17 | 15 | 13 | 12 | 63 1 | 69 6 | 1 | 1 | 11 | 57 9 |
| III | 43 | 28 | 12 | 7 | 6 | 6 | 14 0 | | | 3 | 3 | 69 |
| IV | 54 | 17 | 7 | 3 | 3 | 2 | 3 7 | | | 0 | 2 | 3 7 |
| Total | 120 | 67 | 40 | 29 | 26 | 21 | 20 0 | | 19 1 | 4 | 20 | 166 |

(Courtesy, Surgery, Gynecology and Obstetrics, January, 1937)

Table 5A—Survivals by Clinical Stage—Total 1926 to 1930—Second Method—Long Needles—Low Intensity—Long Intervals

| Stage | Total | 1 | 2 | 3 | 4 | 5 | Per Cent | Per Cent | Opera- bility | Died of Ca in 6th year | Symptom free after 5 years | Per Cent |
|----------|-------|-----|----|----|----|----|-------------|-------------|------------------|---------------------------|----------------------------|-------------|
| | 10 | 10 | 9 | 9 | 9 | 9 | 90 0 |) | ſ | 2 | 7 | 70 0 |
| <u> </u> | 52 | 48 | 35 | 32 | 31 | 28 | 53 8 | 59 6 | { | 1 | 27 | 519 |
| | 62 | 51 | 37 | 24 | 20 | 18 | 29 0 | | | 1 | 17 | 27 4 |
| | 49 | | 0 | 0 | 0 | 0 | 0 0 | \ <u></u> | | 0 | 0 | 0.0 |
| IV | | | | | 60 | 55 | 31 8 | \ | 35 7 | 4 | 51 | 29 3 |
| Total | 173 | 111 | 81 | 65 | 00 | 33 | 310 | | | | | |

Note increase in survival rate Stage III 6 43 to 18 62, 14 per cent to 29 per cent (Courtesy, Surgery, Gynecology and Obstetrics, January, 1937)

Table 6—Survivals by Clinical Stage—Total 1926 to 1928—Second Method 72 to 96 Hours—3000 to 5000 MGM Hours

| Stage | Total | 1 | 2 | 3 | 4 | 5 | Per Cent | Per Cent | Opera- bility | Died of Ca in 6th year | Symptom free after 5 years | Per Cent |
|-------|-------|----|----|----|----|----|-------------|-------------|------------------|---------------------------|-------------------------------|-------------|
| | 4 | 4 | 3 | 3 | 3 | 3 | 75 0 |) | | 1 | 2 | 50 0 |
| | 30 | 28 | 20 | 19 | 18 | 15 | 50 0 | 52 9 | Ì | 1 | 14 | 46 6 |
| III | 29 | 24 | 18 | 10 | 9 | 9 | 31 0 | | | 1 | 8 | 27 6 |
| -IV | 33 | | 0 | 0 | 0 | 0 | 0.0 | | | 0 | 0 | 00 |
| Total | 96 | 58 | 41 | 32 | 30 | 27 | 28 1 | | 35 4 | 3 | 24 | 25 0 |

Note increase in Stage III survivals over 1921 to 1925 group Also decrease in Stage II survivals (Courtesy, Surgery, Gynecology and Obstetrics, January, 1937)

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Table 6A—Survivals by Clinical Stage—Total 1929 to 1930—Second Method 144 to 168 Hours—6000 to 10,000 MGM Hours

| Stage | Total | 1 | 2 | 3 | 4 | 5 | Per Cent | Per Cent | Opera- bility | Died of Ca in 6th year | Symptom free after 5 years | Per Cent |
|-------|-------|----|----|----|----|----------|-------------|-------------|------------------|---------------------------|-------------------------------|-------------|
| I | 6 | 6 | 6 | 6 | 6 | 6 | 100 0 | 67.8 | ſ | 11 | 5 | 83 5 |
| II | 22 | 20 | 15 | 13 | 13 | 13 | 590 | 010 |) | 0 | 13 | 59 0 |
| III | 33 | 27 | 18 | 13 | 11 | 9 | 27 2 | | | 0 | 9 | 27 2 |
| IV | 16 | 0 | 0 | 0 | 0 | <u> </u> | 0 0 | | | 0 | 0 | 0.0 |
| | - | 53 | 39 | 32 | 30 | 28 | 36 3 | | 36 3 | 1 | 27 | 35 0 |
| Total | '' | 33 | 3, | 1 | 1 | | | | <u></u> | | | |

Note increase in Stages I and II survivals Stage III remains about the same (Courtesy, Surgery, Gynecology and Obstetrics, January, 1937)

Table 7—Comparisons of Results in Cancer of the Cervix at Different Clinics

| A. the and almo | Total cases | "Operability" | | all cases ated | | Remarks |
|-----------------------------|-------------|---------------|-------|-------------------|-----------|-----------------------|
| Author and clinic | treated | Per cent | Cases | Per cent | Period | |
| Burnam, 1932 (2) | 262 | 20 6 | 60 | 22 9 | 1925-1927 | |
| Healy, 1928 to 31 (2) | 371 | 28 0 | 97 | 25 9 | 1922 1924 | |
| Schmitz (12) | 607 | 21 0 | 135 | 22 26 | 1914 1929 | Absolute figures |
| Mayo Clinic, 1924 (2) | 1212 | not given | 260 | 20 9 | 1910 1927 | |
| Ward, G G, 1935 (13) | 457 | 20 6 | 111 | 24 29 | 1919-1929 | Absolute rate—treated |
| Heyman, 1932 to 1934 (2) | 1029 | 26 7 | 235 | 22 6 | 1910 1927 | |
| Heyman, 1931 (2) | 270 | 32 5 | 54 | 20 0 | 1918 1920 | Radium alone |
| Regaud, 1932 | 242 | 25.2 | 84 | 34 5 | 1924 1926 | External radiation |
| Lacassagne, 1932 (2) | 243 | 35 3 | | , , , | 1924 1920 | X-ray and radium |
| Regaud, 1932 (2) | 36 | 75 0 | 7 | 19 0 | 1921 | |
| I acassagne, 1932 (2) | 63 | 50 0 | 17 | 26 0 | 1922 | Radium alone |
| Institut du Radium (2) | 74 | 42 2 | 23 | 31 0 | 1923 | |
| Voltz, 1932 to 34 (2) | 720 | 44 0 | 173 | 24 0 | 1924 1928 | |
| Marie Curie-London (2) | 215 | not given | 72 | 334 | 1925 1928 | Radium alone |
| Meigs | 51 | 23 5 | 12 | 23 5 | 1925 | |
| Norris, 1934 | 153 | not given | 35 | 22 8 | 1924 1926 | |
| | 293 | 29 0 | 79 | 26 9 | 1921-1930 | Absolute figures |
| R I Hospital | 120 | 19 1 | 24 | 20 0 | 1921-1925 | Radium alone |
| Pitts and Waterman, 1936 | 96 | 35 4 | 27 | 28 1 | 1926-1928 | |
| | 77 | 36 3 | 28 | 36 3 | 1929-1930 | |

(Courtesy, Surgery, Gynecology and Obstetrics, January, 1937)

especially of the stage three (Schmitz) group, and that these results have been obtained without undue immediate mortality or without increasing the incidence of fistula formation"

CANCER OF THE UTERUS

W E Costolow²⁰ reports results in 1143 cases treated by Soiland, Meland and himself between the years 1921 and 1934. The treatment in the earlier cases was inadequate according to the standards of today. In the period from 1926 to 1930 the amount of primary regression, palliation and the percentages of cures increased. Larger doses of radium, with heavier filtration, were given. Also x-ray treatments were given in a systematized method with a 200 Kv P machine.

In primary carcinoma of the cervix, there is a five-year survival of 58 cases out of a total of 298 cases seen. This total includes cases not treated and others untraced. This is a five-year survival of 195 per cent.

Costolow discusses the progressive stages of earlier irradiation treatments and then gives the following detailed account of his present method

Present Technic-Since 1933 in our present technic, a voltage of around a half million is used with the Lauritsen type tube-distance 52 cm, filter 06 mm lead (equivalent 12 mm or ½-inch copper), effective wave length 005 Ångstrom, half value layer 05 mm lead, in aluminum, half value layer 23 mm aluminum, depth dose 53 per cent at 10 cm (in paraffin) Treatment rate is 15 r per minute. Four or six pelvic portals are used, two 15 by 15 cm portals anteriorly over the pelvis, two 15 by 15 portals posteriorly, and two laterally, if six portals are used Daily, two portals receive 150 r units (measured in air), total dosage of from 1600

to 2000 r is given each portal. This produces a definite erythema with desquamation. Diarrhea is complained of in many cases but usually soon disappears if the daily dosage is decreased. In some cases 300 r is given daily, alternating the four or six portals. With safety, from 10,000 to 12,000 r units may be given over a period of from five to six weeks. The plan of this treatment should be individualized considerably, according to the size of the patients and their ability to withstand the irradiation.

The primary growth is markedly influenced by x-ray series. Often, a cauliflower primary growth of a high degree of malignancy will completely disappear after such a series.

Following the x-ray series, radium applications are commenced immediately, a divided series of vaginal and intrauterine applications being given. In the vaginal application, 2 mm of gold and 1 mm of aluminum filter is used, and in the intrauterine application, 1 mm of gold and 1 mm of aluminum is used Previously, we applied a vaginal dosage of from 1200 to 1400 milligram hours and an intrauterine dosage of from 900 to 1200 milligram-hours. This was repeated in one week and again in two weeks. Since the supervoltage x-ray has been used, we have reduced the vaginal vault dosage but have not eliminated it Usually, however, most of the radium dosage is given intrauterine With 1 mm gold filter, a dosage of from 4000 to 6000 milligram-hours may be given This dosage is divided into one- and two-week intervals Many cases which have had the full radium dosage have not shown any bad effects following this heavy irradiation. The fact that the radium follows immediately after the x-ray series is probably the important factor in preventing unduly delayed reactions, because the tissues in the vaginal

vault and cervix have not had time to develop fibrosis and interference with the local circulation, which occur from four to six weeks following intensive irradiation

Certainly, the intrauterine radium can do no harm to the bladder or rectum, as distance and filtration prevent much irradiation outside of the walls of the uterus. We believe the radium dosage absolutely essential in order to give sufficient irradiation to the uterine canal and cervical glands.

Radiumhemmet Experience in Postoperative Radiological Treatment of Cancer of the Corpus Uteri

A report by Heyman²¹ covers a series of 65 cases of cancer of the body of the uterus In every case the diagnosis was verified by histological examination The evidence is also complete as to the condition of the patient at the end of the fiveyear period Of these 65 patients, 52 had total hysterectomy and 13 subtotal hysterectomy The postoperative irradiation consisted in most cases of one vaginal radium application of about 2000 milligram-hours followed by deep roentgen rays. The treatments were given through two anterior and one or two posterior portals. In the course of 9 to 12 days, each portal was given three treatments ot 400 r, making a total of either 3600 or 4800 r

Heyman has considered his results in painstaking detail with regard to recurrences and their intervals following operation. He is of the opinion that better end results are obtained if postoperative irradiation is begun within four weeks than if it is postponed for a longer time. Of the 65 patients covered in this report, 51 were alive and free from symptoms five years after the beginning of treatment or five-year cure of 78 5 per cent.

CARCINOMA OF THE OVARY

Results Obtained by Radiation Therapy — Carcinoma of the ovary is one of the most radiosensitive epithelial tumors The treatment given by Jacobs and Stenstrom²² varied considerably in individual cases and is described as belonging to three classes Small, medium and large A small dose was 50 per cent S E D or less to each of two fields or equivalent A medium dose was 50 to 100 per cent S E D to each of two fields or less than 60 per cent S E D to each of four fields A large dose was more than 100 per cent S E D to each of two fields or more than 60 per cent S E D to each of four fields The maximum amount of radiation in any one course was 140 per cent S E D to each of four fields in three weeks' time The maximum number of courses to any patient was four Many of the patients received from 100 to 130 per cent S E D to four fields in two This latter dosage and a half weeks was the course usually planned

The physical factors used were 200 Kv P mechanically rectified, 30 ma, 70 cm S T D (60 cm on lateral fields), 1 mm copper and 4 mm aluminum filter. The output of the tube was 15 may per minute at 70 cm and the effective wave length 0.16 Ångstrom units. Under these conditions 1 S E D for a large field is approximately 700 m. The treatment was delivered through large portals, 350 to 500 sq cm anteriorly and posteriorly and from 200 to 300 sq cm laterally.

In the series reported there were 59 cases of carcinoma of the ovary. There were nine cases given small and medium dosage but none survived. In the other 50 cases given large dosage, 32 per cent survived for five years or more.

This seems to be direct evidence that large amounts of x-ray dosage, repeated

over a considerable interval of time, is necessary to cure carcinoma of the ovary Evaluation of the degree of palliation secured in those patients who died is not possible, but the authors state that it is a very real amount. Some patients had from a few months to several years of normal life before a recurrence finally led to invalidism and death. Only a few advanced cases failed to receive any benefit from their treatment.

UTERINE FIBROIDS23

Evaluation of Irradiation in Treatment-Uterine fibroids are not malignant but sarcomatous degeneration may take place in a small percentage of them Some women with fibroids develop cancer of the cervix or of the body of the uterus but the author contends that this does not happen any oftener than in women without fibroids Fibroids are much more common in women over 40 years of age than in younger women Many fibroids of the uterus never give any symptoms requiring treatment. In such cases they usually shrink and may even disappear after the menopause The indications for treatment are severe bleeding with secondary anemia and pressure symptoms on neighboring organs due to the size of the tumor

If the tumor is no larger than a three months' pregnancy, it is usually possible to determine whether or not other conditions are present as complications. If the tumor is larger than a three months' pregnancy, the chances are greater that complications are present and an exploratory laparotomy should be done. If laparotomy is done, the treatment might better be continued by surgical measures rather than by irradiation.

Uterine fibroids are a predisposing cause of sterility, though they do not always prevent pregnancy. If the birth

of a child is of paramount importance operative procedures are more likely to be successful than irradiation because heavy enough dosage to cause regression of the fibroid is likely to put an end to the functional activity of the ovaries. In cases where the birth of a child is not of paramount importance, the treatment should aim to produce a permanent artificial menopause. External roentgen irradiation is preferable to intrauterine application for the following reasons.

- 1 It is applicable to more cases
- 2 It is less likely to be followed by complicating reactions
 - 3 It is less trying on the patients

Roentgen irradiation is more economical than the external use of large amounts of radium by teleradium ther-One of the chief advantages of surgery in the treatment of uterine fibroids is that a prompt cessation of bleeding results, whereas this is not quickly accomplished by irradiation Among the disadvantages of surgery may be mentioned its great first cost, and the prolonged disability of the patient The greatest disadvantage of surgery is the attendant mortality. The actual death rate is hard to determine because it varies so greatly according to circumstances It depends upon the skill of the operator and his good fortune in avoiding infection, and upon the general condition of the patient and the size of the tumor Reports on series of 100 or more cases have shown death rates of from one to five per cent

In the author's experience with 1800 cases of uterine fibroids treated by irradiation, there has not been a single death due to the treatment

The author has studied a series of 100 consecutive cases from the standpoint of the end results. In 59 cases the tumor has entirely disappeared and in 32 it has been reduced greatly in size. In the re-

maining nine cases there was no reduction in size of the fibroid but on the other hand there has been no increase in size over a period of several years

In all cases the bleeding was controlled and a complete amenorrhea established. The average time for the establishment of the artificial menopause was five and one-half weeks, but in some cases the time was as long as four months

Hot flushes were severe in four cases and caused the patients considerable dis-Moderate hot flushes with comfort sweating occurred in 34 cases Mild hot flushes occurred in 58 cases but did not worry the patients at all The average duration of the hot flushes was 11½ months, the minimum duration was one month, and the maximum three years The author's conclusions in part are as follows

"The production of the artificial menopause does not produce serious or persistent physical or mental changes of any kind A great many patients volunteer the information that they feel a great deal better after the treatment than they have felt for years In this connection, it may be recalled that formerly it was frequently observed that when the natural menopause was reached, a great many patients felt in better health, stronger and more active than they had been for some years prior to this event This is, of course, against the normal developments in advancing age Older persons do not feel better than younger persons, naturally There is evidence, therefore, that the ablation of the ovarian function may be helpful rather than harmful in the general feeling of well being It is hardly necessary to refer to the frequent nervous and psychic disturbance of mild character that occur during menstrual life and are directly associated with menstruation Certainly we have seen no development of the

nervous conditions to which some authors refer In addition to the safety in irradiation to produce the artificial menopause in healthy women, it seems also safe to employ the same measure in psychoneurotics where the local indications for treatment are urgent It must be remembered, however, that this class, and even normal patients, can be given a great deal of worry if adverse criticism is made of the treatment they have had, or if the physician himself, who is giving the treatment expresses anxiety as to the consequences on the physical or psychic well being of the patient"

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THE INJECTION TREATMENT OF HERNIA

By Frederick A Fiske, M D

Introduction — The historical background, the experimental work, the selection of cases, the solutions, the truss, the technic, the after treatment, the complications, and the statistical reports concerning the injection treatment of hernia has been covered by Fiske and Genkins, Cyclopedia of Medicine, XIII, 267 to 270, 1936 This article will serve as a supplement in view of the recent work without attempt to fully cover the subject For more complete information one should consult C O Rice's "Injection Treatment of Hernia" (F A Davis, 1937)

O H Wangensteen¹ states "Time will ultimately judge impartially of the merits of the injection method of treating hernia. When the question of the best sclerosing agent has been settled and the technic of the procedure has become standardized, and when sufficient trial in practiced hands has adequately shown that selected herniae can be satisfactorily treated by injection without recourse to operation, surgeons generally will probably welcome this means as a valuable addition to the acceptable methods of dealing with hernia."

Selection of Cases — Only those hermae which are completely reducible and maintainable by truss pressure in all positions should be treated by injections. It is generally agreed that sliding herma, herma associated with undescended testicle, incarcerated and strangulated herma are definite operative cases. A F Bratrud² feels that large scrotal hermae give doubtful results and should be operated upon. According to him, if there is any suggestion of an impulse or the hermae comes down occasionally after fitting of a truss, the case should be

operated upon, not injected While a few femoral herniae have been successfully treated by injections, Bratrud feels that there are liable to be complications Our personal feeling is that these should never be treated by injections; since proper truss pressure cannot be safely applied in the cases of femoral hernia 3 Hemophilia, diabetes, hyperthyroidism³ contraindicate the treatment inguinal herniae with external rings larger than 3 cm are excluded from treatment by injections by C O Rice 4 He includes excessive obesity, all conditions which cause abnormal intra-abdominal pressure, and chronic cough among the contraindications for injections

Solutions-At present there is no universally accepted sclerosing agent After considerable clinical and experimental study, A F Bratrud (ibid) feels that the best results follow the use of Proliferol and the phenol-thuja mixture Injections of each solution at different sites at the same time or the addition of two drops of the phenol-thuja mixture to 1 cc of Proliferol are advised The use of these solutions requires preliminary anesthetization with 2 cc of two per cent novocam The use of the local anesthetic preliminary to the injection, has been considered inadvisable by C O Rice (loc cit) since it may disguise the pain produced by misplaced injections into the peritoneum or the vas deferens He prefers the mild soap solution (Sylnasol)

H. I Biegeleisen⁵ demonstrated the diffusion of solutions injected in the region of the internal ring by using 5 cc of dilute Diodrast and taking roentgenograms From this it seems that the cord, peritoneum, nerves, and epi-

gastric vessels are necessarily brought in contact with the injected solution. It is therefore imperative, that the irritant should not be destructive in character. He has used *Sylnasol* with safety in five and seven and one-half per cent concentrations, average dosage 3 cc. The symptoms of mild shock subsiding in 30 minutes or less due to penetration of the parietal peritoneum with Sylnasol was observed in four instances by Bie-

will be marketed under the name of Monolate

In England, Maurice Lee⁶ uses a solution made of equal parts of *quinine-urethane* and *lithocaine* (lithicum salicylate plus tutocaine)

Truss—The importance of a properly selected and properly fitted *truss* cannot be too strongly emphasized. An improper, poorly fitted truss will almost certainly result in failure to cure hernia,

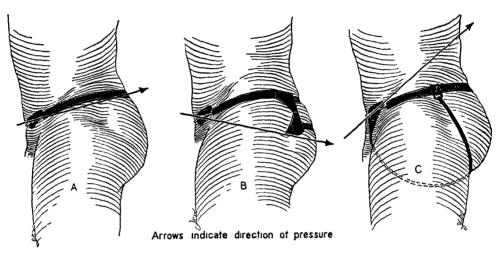


Fig 1—Diagram to show the direction of pressure exerted through the inguinal canal by various types of trusses. A, Rigid Truss. Posterior counterpressure too high. The line of force travels upwards and reduces the efficiency of the truss. B, Semirigid Truss. Correct posterior counterpressure. Line of force at right angles through inguinal canal. C, Spring Truss. Posterior counterpressure too high. The leg strap pulls the upper portion of the pad outward, thus directing the line of force so high that the pressure over the internal ring is negligible. (Courtesy Amer Jour Surg., May, 1937.)

geleisen No permanent ill effects followed

Monoethanolamine Oleate solution has been used in two strengths, two and one-half per cent and five per cent, without untoward effects by Biegeleisen Intraperitoneal injection occurred a few times producing symptoms similar to those observed with Sylnasol, again no permanent ill effects were observed after these accidents. The initial dose is ½ cc of two and one-half per cent solution gradually increasing ½ to 1 cc per injection to a 5 cc total. He has used 5 cc of the five per cent solution.

regardless of the technic of injection or the solution used, while cases of apparent cure of herma have been known to occur by prolonged and proper truss pressure alone

F I Harris and A S White⁷ have presented the anatomical considerations of the inguinal area in relationship to truss requirements. They state that the important factors to be considered in the selection of a truss to be used for injecting a hernia are (1) Its accurate placement over the internal ring in an indirect hernia, and over Hesselbach's triangle in a direct hernia, (2) the

necessity of pressure through the inguinal canal by means of a low posterior fulcrum at right angles to the truss pad (Fig 1), and (3) the necessity of having the truss pad on a line with the encircling band of the truss A complete description of the common varieties of trusses is detailed and illustrated The efficiency of each type of truss is tabulated with regard to its adaptability for the injection treatment of hernia They prefer the

larger and thicker pad than the average individual.

Diagnosis—The importance of accurately distinguishing between the direct and indirect type of hernia is very important from the standpoint of truss pressure as well as variation in the technic of placing the injections. In addition to the usual differential factors used in the diagnosis, F I Harris and A S White (ibid) found a definite relation-

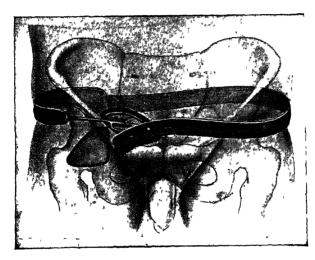


Fig 2—Unilateral Semirigid Truss with single strap, front view Note—(1) The correct placement of the encircling band at the area of least movement about the hips, halfway between the crest of the ilium and the trochanter of the femur (2) The correct relationship between the pad and the encircling band (3) The beveled sponge rubber anatomically correct pad (Courtesy, Amer Jour Surg, May, 1937)

single or double strap semirigid type of truss (Figs 2, 3, 4), but accept the adaptability of the rigid types, especially the single or double strap types with bilateral low counter pressure (Fig 5)

According to Bratrud (*ibid*) any type of truss can be used provided it holds the contents within the abdomen For a single herma a spring truss is more comfortable than a band truss For a double herma the band type truss gives the best results

F S $McKinney^s$ feels that a correct pad is just as important as the truss itself. The obese patient requires a

ship between the length of the inguinal ligament and the type of hernia. In a series of 300 patients it was found that when a hernia is present in a person whose inguinal ligament measures less than 15 cm it is always the indirect type, and when it measures more than 15 cm it is the direct type. It was likewise observed that the length of the penis varies inversely with the length of the inguinal ligament.

Complications—Seventy-eight of the 445 cured hermae reported by C O Rice⁹ developed the following complications induration of the cord, 44,

superficial ulceration of the skin due to truss irritation, eight, severe pain suggesting peritoneal irritation, ten, chemical peritonitis, two, hydrocele of the cord, seven, local abscess, two, dermatitis, one.

While F. S McKinney gives swelling of the cord as the most frequent complication, it is interesting to survey the case reports of the five patients hospitalized (1) Patient, age 76, had a large scrotal hernia which had been present 30 years. The hernia strangu-

tion made into the sac Swelling of scrotum Hospitalized five days Complete recovery There were no deaths in the 700 cases either directly or indirectly due to the injections, however, he reports a death due to perforation of the ileum which was admitted to the hospital after injection outside

The question of sterility and impotence as a complication of the injection treatment has been reported by C E Rea¹⁰ as unimpressive. In a series of 26 bilateral inguinal hermiae followed up to three

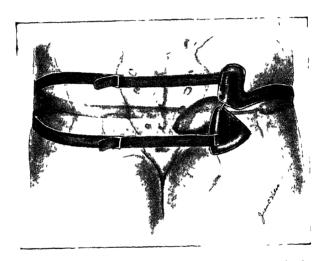


Fig 3—Limitateral Seminigid Truss with double strap, back view (Courtesy Amer Jour Surg, May, 1937)

lated following the fitting of a truss He had no injection Operation Recovery (2) Patient developed a severe pain in back and side following injection slough (size of dollar) opposite umbilicus from injection of deep epigastric artery Slough healed in three weeks (3) Patient had symptoms of local peritonitis (nausea and vomiting) following injection of recurrent hernia Operation Small area of peritonitis found Repair of hernia, uneventful recovery (4) Patient with abscess following injection for a recurrent hernia after appendectomy Drained three weeks Recovered Patient with large scrotal hernia Injecyears, ejaculation tests were performed in 15 cases, all of which showed normal fertility. Two patients, both of whom showed abnormal mental traits, complained of less libido, three months and five years after the hernial injections. In a series of 75 unilateral inguinal herniae, followed up to two years, only one complained of less libido. He feels that fear of sterility or impotence should not deter employment of this therapeutic measure

S A Zieman and T M Larkowski¹¹ found necrosis of cord structures after one injection of the tincture of Thuja solution in the region of the right internal ring. Operation two weeks after the in-

jection showed healthy tissues to and including the aponeurosis of the external oblique Exposure of the inguinal canal revealed a gangrenous strip including fibers of the internal oblique and cremasteric muscles, the upper pampiniform

injection method must be decided by constant careful case reports over a long period of years. The report of 100 cases by F I Harris and A S White¹² were eminently satisfactory; however, these were not followed long enough to be con-

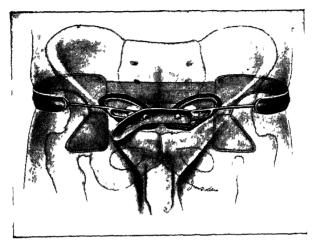


Fig 4—Bilateral Semirigid Truss with single strap, front view (Courtesy, Amer Jour Surg, May, 1937)

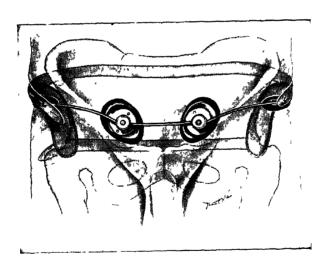


Fig 5—The Frame Truss with bilateral curved posterior fulcrum and double strap, front view (Courtesy Amer Jour Surg, May, 1937)

plexus and the greater part of the cord The vas was blanched, swollen, and tortuous, running directly through the gangrenous spots An uneventful convalescence followed the surgical repair

End Results—Proper evaluation of the efficacy of treating hernia by the sidered a final result. The difficulty of obtaining adequate follow-up has been indicated by N. N. Crohn 13

In a series of 300 cases from the Hernia Clinic of the University of Minnesota, F S McKinney¹⁴ reports 83 per cent cures and 17 per cent failures Many

of the earlier cases had a recurrence, which usually responded to further injections, and at times a change of the type of truss. It was found that the average number of injections required was greater than usually considered necessary. The majority of the failures in this group were in patients over 50 years of age.

From a study at the Minneapolis General Hospital, C O Rice¹⁵ states that cures were obtained in 379 patients with 445 herniae. There were 11 failures No patient was pronounced cured until the check-up examination revealed "no impulse" for a period of six months after the last treatment and until the patient has been without his truss for at least four months. No deaths occurred in any of the treated cases. If only the controlled cases are calculated, Rice states that the percentage of cures is 97.6

C G Burdick and B L Colev¹⁶ report a most discouraging group of cases. In a series of 66 cases with 92 hermae, only 11 cases were apparently cured, and of these nine were still wearing trusses. Several solutions were used, and they feel that the injection seems reasonably safe. They state, "Until statistics are forthcoming that point to a much higher curability of herma by the injection method than we have been able to obtain at the Hospital for Ruptured and Crippled, we have definitely decided to abandon the method entirely."

Of 350 cases examined by W M McMillan and D R Cunningham, 17 308 were found suitable for treatment. One

hundred and seventy were still under active treatment and 138 were discharged completely cured. The remaining 42 patients failed to co-operate. They found a recurrence rate of eight per cent.

In 100 cases treated by injections, D E Ross¹⁸ reports 60 cured by one course, 11 by two and 20 still under treatment There were failures in eight and three ceased treatment One death occurred a few minutes after injection which was found at necropsy to be caused by a coronary thrombosis

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OPHTHALMOLOGY

Review of Medical Progress*

Conrad Berens, M D and Joshua Zuckerman, M D

New concepts, new methods of diagnosis and new methods of medical and surgical treatment of eye diseases have been advocated within the last few years. These topics may be summarized under separate headings in the following way.

- 1 New Concepts—The etiology of cataracts has been ascribed to deficiency of vitamin A, excessive sugar, disturbed calcium metabolism, loss of cystine from the lens and toxic disturbances ¹
- 2 New Methods of Diagnosis—The use of the gonioscope for examining the angle of the anterior chamber is gradually being accepted as a valuable aid in the detection of anterior synechiae which are one of the first signs of glaucoma

For diagnostic purposes, uveal pigment has been injected intracutaneously in cases in which the diagnosis of sympathetic ophthalmia was doubtful

Allergy has been stressed as an etiologic factor in vernal catarrh, some forms of iritis and even in some cases of detachment of the retina ²

Viruses have been studied in relation to several eye diseases and the generally accepted opinion is that a virus is the infectious agent in trachoma

In immunology, vaccines and filtrates made from cultures taken from the intestinal tract, nose, throat, teeth or tonsils, have been used in diagnosis and administered in the treatment of acute and chronic diseases of the eye

3 Treatment—(a) Medical Treatment—Artificially induced fever therapy for acute infections of the eye, especially gonorrheal infections and for the treatment of cerebrospinal syphilis has proved beneficial.

In the treatment of syphilitic atrophy of the optic nerve, if not too far advanced, induced *malaria therapy* has been of benefit^{3, 4} and the instillation of *miotics* or operations for decompression of the eye⁵ (*cyclodialysis* alone or combined with *iridenclessis*) have been used with good results. Moreover, in optic atrophy regardless of etiology, retrobulbar injections of 8 minims (0.5 cc.) of a solution of *atropine* 1, 1000 have been advocated by G. Springowitsch⁶ and inhalations of *amyl nitrite* by V. Much ⁷

Experimental investigation of the value of vitamins in the prevention and treatment of diseases of the eye has proved that *pure vitamin A* (or cod liver oil) when applied locally, stimulated rapid regeneration of the epithelium of the cornea in rabbits ⁸ (The vitamin D contained in the cod liver oil had no effect) Hemorrhages in the vitreous may result from a lack of vitamin C ⁹ Administration of vitamin A for the treatment of superficial punctate keratitis in three patients effected a cure ¹⁰

(b) Surgical Treatment—The use of corneal grafts taken from the eyes of stillborn fetuses, has proved to be of assistance in maintaining transparency in corneal transplants

^{*} Aided by a grant from the Ophthalmological Foundation, Inc

Improved methods of surgical procedure have been devised for detachment of the retina

Special surgical instruments for use in conjunction with gonioscopy to open the canal of Schlemm have been designed by Barkan.

Hildreth recommends the use of a fluorescent lamp in cataract extraction particularly for cases in which the lens has been dislocated into the vitreous. This lamp renders the surface of the lens and the particles of the cortex fluorescent so that delivery may be effected more readily.

Aniseikonia - Correction - Of a series of 34 patients examined by G Hardy,11 for whom iseikonic lenses were indicated either for relief of symptoms or for aniseikonia or for both, 41 per cent were improved after wearing them and 41 per cent were unimproved The effect in one patient (three per cent) was not reported and 147 per cent were not given lenses Hardy points out that the actual evaluation of these results is difficult because the benefit obtained in some cases may have resulted from a better correction of refraction, improvement of muscle imbalance or from the psychological effect of the impressive examination

The relative sizes of the images of both eyes were examined in 43 enimetropic patients who presented symptoms of ocular disturbance, $c\ g$, headache, ocular pain, ocular fatigue and photophobia 12 Twenty-nine were found to have aniseikonia. Of the 14 patients who were followed and for whom iseikonic lenses were prescribed, ten obtained complete relief from their symptoms

Another group of 288 patients were examined with the ophthalmoeikonometer ¹³ One hundred and twenty-eight patients in this series did not obtain iseikonic lenses. Of 160 who wore isei-

konic lenses, 55 patients were definitely relieved of their symptoms, 44 moderately benefited, 11 were slightly benefited and 50 were unrelieved. Although no definite conclusions are drawn from this study, Berens recommends continued scientific research and clinical investigation in regard to size differences.

Brain Tumor

Optic Radiation — Diagnosis — Eleven cases which presented an unpaired crescentic or hemicrescentic defect in the periphery of the temporal field of vision (of one eye) arising from a lesion of the optic radiation of one side are reported by M B Bender and I Strauss ¹⁴ It is pointed out that this temporal scotoma is of early diagnostic value in localizing a brain tumor which involves the optic radiation

Suprasellar Meningioma-The ocular signs in 21 cases of suprasellar meningioma are described by E Hartmann and L Guillaumat 15 All the cases presented optic atrophy or papilledema, reduction in visual acuity and extensive defects in the field of vision In 15 cases. bitemporal defects were encountered, in one case, homonymous hemianopia, in a second case, horizontal hemianopia and in a third concentiic contraction with central scotoma. One case of atypical and another of typical, Foster Kennedy syndrome were also diagnosed ment in visual fields accompanied by some improvement in visual acuity occurred in 14 patients who survived operation

Campimetry

Myopia—F Ziering¹⁶ examined the blind spots of 15 myopic patients. In all cases when correction was not worn, the blind spot was enlarged temporally and upward but these enlargements disappeared when correction was worn. To avoid misinterpretation of the findings,

correction should be worn when campimetric studies of myopic patients are made

Caruncle

Cancer — Treatment — For nevoid cancer of the caruncle, F. Terrien and P. Veil¹⁷ urge early exenteration of the orbit and point out the futility of radium Their opinion is based on a case in which a painless, small, hard, nonadherent nodule was found at the inner canthus of the eye, in a woman, 70 vears of age Excision revealed nevus cells without much pigment and no After recurrence, radium metaplasia was applied Exenteration was advised but was refused until six months later, when, after local extension into the orbit, subperiosteal exenteration was per-Histological examination reformed vealed an alveolar architecture with melanophores Metastasis to the spine resulted in death several months later

Melanoblastoma—Twenty-nine cases of pigmented tumor of the lacrimal caruncle reported in the literature are discussed by J. O. Wetzel ¹⁵. He also described in detail one case examined by him

Eight years before examination a man, 76 years of age, noticed a brown staining of the caluncle, several months after having spattered some hot grease in his eye. Seven years after the injury, the mass began to grow rapidly and the patient experienced difficulty in completely closing his eye.

Examination revealed the presence of a brownish-black pedunculated tumor, the size of a grape, with neoplastic invasion of the conjunctiva of the eyelid and eyeball as well as pigmentary infiltration of the sclera. Histologic examination of the enucleated eye revealed a polymorphous-celled melanoblastoma of a highly malignant type.

Choroid

Choroideremia — Symptoms — The literature on choroideremia is reviewed by A. J. Bedell, ¹⁹ who also reports five cases. The condition is characterized by bilateral loss of the choroid accompanied by hemeralopia and contraction of the field of vision. Central vision is retained until very late in the course of this condition. The choroidal vessels are small and straight or are entirely absent. Choroideremia usually occurs in males.

Miliary Tuberculosis — A Hudelo and J Voisin²⁰ report a case of miliary tuberculosis of the choroid in a man, 36 years of age, whose condition was erroneously diagnosed as alcoholism and septicemia It was only as a result of ophthalmoscopic examination that the diagnosis of miliary tuberculosis was made

Conjunctiva

Conjunctivitis—Allergic—According to A C Woods, ²¹ allergic conjunctivitis is manifested as a transitory conjunctivitis with edema and chemosis, a chronic blepharoconjunctivitis with eczema or as a chronic recurrent conjunctivitis with folliculosis and blepharitis

He points out that certain forms of recuirent iritis and iridocyclitis may be manifestations of allergy. Specific skin hypersensitivity is diagnostic. Elimination of the offending allergen or specific desensitization is the treatment suggested.

Allergic conjunctivitis occurring in two patients suffering from urticaria is reported by A Lundberg ²² One was a contact conjunctivitis, resulting from contact with the shell of a crab, in a patient who was allergic to crabs and lobsters. The other occurred in a patient who had erythema nodosum

Gumma; Congenital Syphilis — Diagnosis—A case of gumma of the bulbar conjunctiva occurred in a girl, 15 years of age, who had congenital syphi-

lis ²³ The diagnosis was based on the appearance of the diseased area, the presence of gumma in other parts of the body and on the family history. There was no involvement of the cornea or sclera

Mucous Membrane Grafts—Treatment—Mucous membrane grafts taken from the buccal mucosa of the mouth are very satisfactory for the correction of defects in the conjunctiva ²⁴ Spaeth advocates their use in the correction of posterior symblepharon, defects in the upper palpebral conjunctiva and in the bulbar conjunctiva following removal of pterygrum, deformities resulting from trachoma, traumatic entropion, coloboma of the eyelid and essential shrinking of the conjunctiva (pemphigus)

After the intact conjunctiva has been released by incision, it is undermined, all scar tissue is resected, and the distorted tarsus is straightened by through and through incisions. A pattern of the defect is made with oiled silk and a graft of mucous membrane is made to match it in shape and size. Injury to the parotid duct should be carefully avoided. The graft is placed with its epithelial surface down on a moist towel, and dissected until only thin mucous membrane remains. It can then be utilized as indicated for various conditions.

Seborrheic Blepharoconjunctivitis — Treatment—The treatment of seborrheic blepharoconjunctivitis is discussed by W B Clark²⁵ He points out that, unlike blepharitis marginalis, this condition occurs in adults and begins in the Zeiss (sebaceous) glands of the cilia and in the meibomian (sebaceous) glands of the tarsus

This disease is characterized by itching, burning and foreign body sensation and may be accompanied by styes, infected chalazia, chronic conjunctivitis, loss of cilia and seborrhea and alopecia of the scalp Local and general treat-

ment for a prolonged period of time are required to effect a cure Local treatment consists of epilation of the infected cilia, expression of the meibomian glands, irrigation of the conjunctival sac, rubbing of the eyelid margins with antiseptic solutions and ointment, instillation of suprarenin (mxxv [15 cc] of a 1 1000 solution to one ounce of a two per cent solution of boracic acid) and in intractable cases, small doses of x-ray.

General treatment consists of refraction, correction of heterophoria, anemia and low metabolic rate, administration of cod liver oil and brewers' yeast, elimination of foci of infection, and treatment of the associated seborrhea of the scalp and eyebrows

Trachoma — Etiology — From their experimental work over a period of six years, L. A. Julianelle, R. W. Harrison, and M. C. Morris²⁶ conclude that (1) in monkeys, malnutrition is not a predisposing factor to trachoma, (2) trachoma does not present any characteristic flora, (3) the infectious agent, which is difficult to filter, can be cultivated by tissue culture, and (4) the agent is a virus of an unusual type

Cornea

Acne Rosacea Keratitis — Therapy —T K Krylov²⁷ reports that subconjunctival injections of mercury oxycyanide are of assistance in the therapy of acne rosacea keratitis

Keratitis—Vitamin A—An ointment containing vitamin A is recommended by E. Heinsius²⁸ for the treatment of erosion of the coinea, bullous and neuroparalytic keratitis and keratoconjunctivitis

He employs a two per cent "vogan" ointment about three times a day, the vitamin A content of which corresponds to a good preparation of cod liver oil (750 international units)

Keratoconus—A case of keratoconus was successfully treated by H L Hilgartner, Henry L Hilgartner and J T Gilbert²⁹ by the administration of thyroid, radium and short-wave diathermy

A girl, 18 years of age, complained of blurring and distortion of vision of the right eye. She had been treated for allergy to foods and for hypothyroidism. A diagnosis of keratoconus had been made several years before. Examination revealed the presence of advanced keratoconus in the right eye with opacification of the apex of the cone. The cornea of the left eye showed a slight conical formation but vision was 20/65 with correction.

Treatment was as follows Daily short-wave diathermy; instillation of dionin and mercurochrome; radium treatments at weekly intervals for three weeks for three-, four- and five-minute periods, respectively followed by treatments every three or four weeks for a five-minute period, diathermy daily for one month, every alternating day for another month, and twice a week afterward, desiccated thyroid substance beginning with 1 grain (0 064 Gm) and increasing to 4 grains (0 259 Gm) daily

At the end of this period of treatment, the vision in the right eye was 20/49-2 with correction and the basal metabolism increased from -28 to +12. They attribute the successful treatment of this particular case to the combined use of thyroid, radium, and diathermy

Keratoplasty—I F Kopp ³⁰ reports that five of his series of 11 cases of transplantation of the cornea have remained permanently transparent. He concludes that to obtain transparent grafts, the presence of normal corneal fibers in the scar is necessary and that the underlying processes responsible for the opacification of the cornea must be

quiescent before transplantation is performed Because anterior synechiae produce opacification of the graft, he recommends their removal by preliminary iridectomy

Phototherapy—Experimental—As a result of an experimental study, M Karbowski³¹ concludes that more rapid healing of the cornea takes place in red than in blue light. The experiment consisted of exposing rabbits' eyes to red and blue light after having experimentally burned or eroded the epithelium of the cornea.

Serpiginous Ulcer—Prophylaxis—During a period of two years, F A Hamburger³² treated all cases of injury of the cornea with two per cent collargol ointment and found that serpiginous ulcer developed in only one case. This particular case was not seen until 24 hours after the injury. He believes that collargol ointment possesses a distinct prophylactic value in these cases.

Diathermy

Diathermic coagulation in ophthal-mology is discussed by M Klein ³³ He also described a new apparatus for the measurement of the resistance in tissue under treatment by high frequency current According to Klein, the dosage can be specified and adjusted provided the proper type and shape of electrodes are employed

During surface coagulation, the region of the eye being treated should be kept moist to avoid carbonization. Carbonization not only prevents diathermic coagulation from spreading into the deeper layers but also allows the production of sparking which may injure the eye.

Drugs

Adrenalin Chloride—Indications— O Barkan and S Maisler³⁴ report that instillation of a solution of adrenalin chloride 1:100 was satisfactorily employed as a substitute for an adrenalin chloride solution of 1 1000, which is usually injected subconjunctivally or applied topically in the form of saturated pledgets, and for glaucosan and suprarenın bitartrate. The authors explain that concentrated adrenalm chloride acts in the following manner (1) It reduces the intra-ocular tension by constriction of the vessels and by causing diminution of secretion (2) By arresting exudation, it prevents blocking of the trabeculae at Schlemm's canal (3) It produces a shrinking of the root of the iris and of the ciliary body so that in spite of mydriasis the filtration angle is maintained free and the formation of adhesions between the iris and the wall of the angle is prevented

A solution of 1 100 of adrenalin chloride has been found of especial advantage in secondary glaucoma following uvertis, as a mydriatic in cases of suspected glaucoma and detachment of the retina as well as in acute and subacute iritis. When this concentrated solution is administered, the patient must be observed constantly because an initial rise in intra-ocular tension may occur.

Epinephrine—Indications—According to M Wiener and B Y Alvis³⁵ a strong solution of *epinephrine* is valuable as a therapeutic agent in many eye conditions

The following findings are reported by the authors (1) In acute glaucoma, epinephrine occasionally produces a decrease in tension after two hours (in some cases, an increase) (2) In chronic simple glaucoma, for which miotics, are required over a long period of time, epinephrine is valuable (3) For breaking up adhesions in cases of iritis and uveitis, it is of extreme benefit as an adjuvant to atropine (4) For controlling tension after operation for glaucoma

and after needling of cataracts and of secondary membranes, epinephrine may be administered alone or in conjunction with miotics (5) Epinephrine is also effective in resensitizing an eye to miotics after miotics have become ineffective

For office and home use, Wiener and Alvis recommend an ointment of two per cent epinephrine bitartrate in tragacanth jelly (a water-soluble base) or in petrolatum and lanolin (an oily base)

Mydriatics; Euphthalmine—A solution of one per cent cocaine hydrochloride plus one per cent euphthalmine hydrochloride is recommended by L T Post 10 as superior to a solution of two per cent suprarenin-bitartrate as a mydriatic except in cases in which extreme mydriasis is required He points out that the effect of cocame hydrochloride plus euphthalmine hydrochloride can be counteracted less painfully, more readily, and more thoroughly. However, an increase in intra-ocular tension may follow its use action by instillation of one drop of a solution of 0.5 per cent eserme is advocated

Syntropan—The use of a solution of syntropan (two per cent) instead of homatropin for dilatation of the pupil is suggested by W Bab ³⁷ The effect of syntropan lasts only a few hours and is readily neutralized by a solution of pilocarpin (two per cent)

Eye in General

Sulfuric Acid Eye-Burns—Treatment—J H Coppez and Brenta³⁸ report two cases of severe burns of face and eyes by a strong solution of sulfuric acid resulting in destruction of the cornea, and a third case in which a weaker solution produced a first degree burn with no loss of vision. They direct attention to Neuman's experiment which demonstrated that the destructive process

continues for several days after the injury and point out that this process can be arrested by removing the necrotic tissue at once, and replacing it with a graft They recommend immediate irrigation of the eyes with water, and early transplants of mucous membrane grafts taken from the lower lip The prognosis should be guarded

Complications — Sinus Operation — The ophthalmic sequelae of radical treatment of the frontoethmoidal sinuses are discussed by P Halbron ³⁹ The lacrimal passages, the eyeball, the eyelids, or the motility of the eyeball may be affected. The action of the superior oblique muscle is most frequently interfered with but other extra-ocular muscles may be involved. Because the resulting diplopia often disappears spontaneously, ample time should be allowed before correcting the diplopia by surgical procedure.

Diabetes—A study of the eyes of 500 diabetic patients by A E Goldfeder and M A Kipelovich⁴⁰ revealed that Intra-ocular tension was below the normal level in 53 per cent, anisocoria was present in 141 per cent, convergence insufficiency occurred in 351 per cent, accommodation was deficient in 706 per cent, refraction was altered in 69 of 100 cases, diabetic cataracts occurred in 35 per cent, retinitis in 18 per cent, xanthelasma in 14 per cent, abducens paralysis in one case and Dalrymple's, Von Graefe's and Stellwagg's signs were found in 66 per cent

Nasal Ganglia—The nasal origin of reflex disturbances of the eyes is discussed by P Halbron ⁴¹ Charlin's nasal nerve syndrome is characterized by intermittent periods of pain, which may last for ten minutes to one hour, inflammation of the eye (ie, iritis, ulceration of the cornea), serous rhinorrhea and tenderness at the nasal portion of the

orbit or at the ala of the nose Immediate relief is obtained by the application of cocaine to the lateral wall of the nose

The sphenopalatine ganglion syndrome is characterized by rhinorrhea, redness and engorgement of the mucous membrane of the nose, accompanied or followed by tearing, photophobia, pain behind the eyeball, in the nose, ear, mastoid region, neck or at the temple Temporary relief follows cocainization of the mucous membrane at the sphenopalatine ganglion. Permanent relief is obtained by correction of the underlying local nasal condition or the patient's general condition

Restoration of Eye Socket-Technic-A method of enlarging an eye socket in cases in which the conjunctiva is deficient is described by J. F S Esser 42 After enlarging the cavity by incising the conjunctiva, a dental wax cast of the new socket is made part of the cast which is not covered by conjunctiva is then covered with a skin graft It is so placed, that when the cast is inserted, the raw surface of the skin will be brought in contact with the raw surface of the socket Removal of the cast after a period of one week reveals that an "epithelial inlay" has been produced

C K Lin⁴³ reports that he successfully restored five of six eye sockets by means of the Wheeler technic. To avoid contraction of the socket, he inserts a small dental-wax mold after the initial large mold has been removed.

Tuberculosis—Diagnosis—Tryptophane Reaction—An experimental study
to determine the clinical value of the
tryptophane reaction as a specific test
for tuberculosis was performed 44 Van
Heuven found that the test is not specific
but merely indicative of increased permeability of the capillaries

Infection of Eyeball; Gas Gangrene—The literature on wound infection of the eyeball resulting from the gas gangrene group is reviewed by H Rieger 45 He also reports five cases Rieger found that most cases of gas gangrene of the eyeball resulted from injury by metallic particles and in some cases contamination with earth and dust Gas gangrene antitoxin was of no value in advanced cases. However, after incision or removal of the infected eye, the general symptoms usually improved rapidly

Plastic Surgery for Hernia of Eyelids—A method for the plastic repair of hernia of the lower eyelids (baggy eyelids) by means of a fascia lata graft is reported ⁴⁶ The transplant is employed to form a new tarso-orbital septum

Hemeralopia; Vitamin A Deficiency—Photometry—According to H Jeghers⁴⁷ hemeralopia is the earliest and most constant indication of a deficiency of vitamin A in adults Photometric studies of 274 adults revealed that a few were deficient in vitamin A Vitamin A deficiency may result from fever, infection, increased basal metabolism, pregnancy, interference with proper absorption of food and from interference with the conversion of carotene or with storage of vitamin A in disease of the liver

Intra-ocular Tension in Pregnancy—E de Grosz⁴⁸ observed a slight decrease in intra-ocular pressure during pregnancy in 105 women. This reduction in tension was attributed to alteration of the pH of the blood, to the action of the pituitary gland and the sympathetic nerves.

Iris

Prolapse — Treatment with Trichloracetic Acid — The effectiveness of trichloracetic acid in the treatment of prolapse of the iris is stressed by J W Bettman and H Barkan ⁴⁹ They

find the following types of cases suitable for this treatment:

- 1. Old prolapses of the iris in which excision or cauterization would produce excessive trauma with severe reaction
- 2 Large prolapse of the iris through the cornea, to which the conjunctiva does not adhere readily.
- 3 Subconjunctival prolapse as a complication in cataract extraction. These cases may be treated several weeks later when manipulation is safe.
- 4 Prolapse of the 111s, not under the conjunctiva (as a sequel to cataract extraction)
- 5 Prolapse of the iris (which recurs during extraction) accompanied by prolapse of the vitreous
- 6 Recurrent blebs of the vitreous which interfere with closure of the wound after cataract extraction

Bettman and Barkan point out the advantages of trichloracetic acid as compared with the use of the actual cautery Because the coagulum produced by trichloracetic acid forms immediately it serves as a guide to the application of the acid Moreover, it acts as a barrier to the entrance of bacteria, while the slough produced by the cautery may favor multiplication of bacteria. The acid produces less reaction and a firmer scar. The following procedure is recommended.

A few crystals of trichloracetic acid are dissolved in one drop of saline solution. After thorough cocamization, the prolapsed iris is dried with a cotton applicator and the eye is held open. A wooden toothpick, previously dipped into the solution, is gently applied to all parts of the exposed iris, or, if the iris lies under the conjunctiva, to the conjunctiva overlying it. After several minutes, the eye is irrigated with saline solution to remove the excessive acid. This procedure is repeated daily for one week.

and then twice a week until the prolapse decreases in size, flattens, and becomes covered with a white eschar.

Leiomyoma — A D. Frost⁵⁰ reported a case of leiomyoma of the iris in a woman, 46 years of age. Only one definite case of leiomyoma has been published previously in the literature. The condition was diagnosed clinically either as an atypical tuberculous nodule or a malignant sarcoma. Microscopic examination of the enucleated eye revealed interlacing closely packed bundles of spindle cells with rod shaped nuclei, arranged like palisades, with eosinophilic cytoplasm and myoglia fibrils characteristic of benign leiomyoma.

Lacrimal Duct

Reconstruction—J Gerke⁵¹ restored a destroyed lacrimal duct by epitheliazation of an artificially produced canal. The vault of the nose is punctured after incision of the mucous membrane, bluntly dissecting toward the eye, and introducing a metal cannula through an incision on the inner surface of the lower eyelid. The cannula is removed after six or eight weeks

Laurence-Biedl Syndrome

Diagnosis—S A Spektor and D D Sokolov⁵² add a case of Laurence-Biedl syndrome to the 73 cases previously reported in the literature. This syndrome is characterized by adiposogenital dystrophy, polydactylism, mental retardation and retinitis pigmentosa.

Lens

Dinitrophenol Cataract — Nineteen cases of bilateral dinitrophenol cataracts occurring in female patients, who ranged in age from 32 to 63 years, are reported by E E Hessing ⁵³ Cataract extraction was necessary

Cataract Extraction — A1r Injection—According to E Selinger⁵⁴ the

injection of sterile air into the anterior chamber after cataract extraction prevents secondary glaucoma. By pressing the hyaloid-iris diaphragm back, air in the anterior chamber prevents prolapse of the iris, and blocking of the angle of the anterior chamber not only by the root of the iris but also by the vitreous, thus preventing rupture of the layer of its anterior border.

Nystagmus

Vertical Reading—A case of vertical reading which occurred in an albinotic patient, 44 years of age, is reported. 55 This patient could read print only if the lines were held in a vertical position, i e., tilted about 90 degrees. Horizontal nystagmus of about 150 oscillations per minute was present Schmidt points out that patients with nystagmus often find that the pseudomovements of printed matter decrease when the head is held in an oblique position

Optic Nerve

Atrophy—Survey—L Lehrfeld and E R Gross⁵⁶ conclude that in spite of treatment, primary atrophy of the optic nerve is progressive. The condition is insidious and by the time blurring of vision is noticed, atrophy is usually pronounced. Early diagnosis and early treatment of syphilis and neurosyphilis are the only means of preventing atrophy of the optic nerve.

The severity of the atrophy of the optic nerve can be determined by the degree of visual acuity which remains, abnormalities of the pupillary reactions warrant thorough investigation and plotting of the fields of vision and examination of the fundus

Lehrfeld and Gross made a survey of 552 patients with primary syphilitic atrophy and 48 patients with secondary atrophy, at the Wills Hopital over a

period of ten years. In 91, conclusive findings were obtained and the balance were tabulated for statistical purposes

Seventy-five per cent of one group of patients, who had received no treatment and who were blind or nearly blind on admission, became blind in less than three years, all became blind at the end of five years Twenty-four per cent of the patients of a group, who had received antisyphilitic treatment, became blind in less than three years, and all at the end of eight years Of 28 per cent of a group, who had received antisyphilitic treatment in addition to fever therapy and subdural therapy, three became blind in less than three years, and all were blind at the end of eight years

Treatment—Atropine—A case of arteriosclerotic atrophy of the optic nerve which was benefited by retrobulbar injections of atropine is reported by F C Cordes ⁵⁷ He recommends from 10 to 15 injections of ½ to 1 cc of a solution of 1 1000 atropine twice a week administered in the manner usually employed for producing retrobulbar anesthesia

Miosis—Cyclodialysis—It has been observed that patients with tabes and optic atrophy often present a low blood pressure ⁵⁸ Lauber assumes that this reduction in pressure is responsible for the production of atrophy of the optic nerve. In his series of 33 cases of optic atrophy, improvement of vision resulted from reduction of intra-ocular tension by means of a miotic or by cyclodialysis. He believes that these measures restore a normal balance between intra-ocular tension and retinal blood pressure.

Hypertensive Meningeal Hydrops —Papilledema—Fifteen cases of hypertensive meningeal hydrops are recorded by L M Davidoff and C G Dyke ⁵⁹ This condition is characterized by increased intracranial pressure (evidenced by headache), papilledema, increased

pressure of the spinal fluid and the abscence of abnormal neurological signs The cerebrospinal fluid is normal The condition is differentiated from fumor of the brain and from adhesive arachnoiditis by pneumoencephalography Pneumoencephalograms reveal the following characteristics The size, shape and position of the ventricular system are normal, the ventricles fill with difficulty and the air escapes into the subarachnoid space during ventriculography Treatment consists of subtemporal decompression and repeated lumbar punctures if decompression proves inadequate

Orbit

Cellulitis in Infancy—G Alamilla and M A Branly⁶⁰ discuss orbital cellulitis in infancy and childhood. They direct attention to the fact that the frontal and sphenoidal sinuses are poorly developed and the maxillary sinuses are incompletely developed in children under seven years of age. In these cases, infection from the ethinoid sinuses is usually responsible for the resulting cellulitis of the orbit. Alamilla and Branly urge not only early incision of the orbit through the lower cyclid but also drainage of the sinuses.

Inflammation — Diagnosis and Treatment—A series of 36 cases of acute inflammation of the orbit with five fatalities (14 per cent) has been tabulated by H Ehlers 61. This series comprising collateral edema of the orbit, subperiosteal or preseptal abscess and phlegmon, arose from infections of the lacrimal sac, the face, sinuses, teeth, and the ear

Ehlers points out that treatment of the causative inflammation is important Surgical intervention for edema is unnecessary and may be harmful Vertical or lateral displacement of the eyeball is suggestive of subperiosteal abscess. This condition requires immediate subperiosteal incision and drainage Opening of the tarso-orbital fascia should be carefully avoided to prevent contamination of the tissues of the orbit. Phlegmon of the orbit is the most serious condition (three of eight cases were fatal). Phlegmon is treated by parenteral injections, antiphlogistic applications, deep incisions and enucleation, if vision is destroyed Vision was lost in eight of these cases.

Infection of Antrum-In involvement of the orbit resulting from diseases of the maxillary antrum,62 extension of infection usually occurs by way of the veins and occasionally by lymphatic or direct extension through the bony wall S10tto points out that the floor of the sinus may present small foramina, and that the floor of the orbit may be connected with the teeth by means of a canal arising from connections between the first and second dentition This developmental and anatomic relationship may explain extension of infection from the teeth to the antrum and to the orbit

Tumor with Buphthalmos—A case of neurofibromatosis occurred in a girl, 6½ years of age 63 She presented evidence of buphthalmos of one eye at birth and had two decompression operations performed on this eye at the age of three weeks and six weeks, respectively Ptosis of the right upper eyelid and enlargement of the right side of the head was observed when the child was about 1½ years of age

At the age of $6\frac{1}{2}$ years, examination revealed that neurofibromatosis involved the right upper eyelid, the temporal and zygomatic areas, lacrimal gland, apex of the orbit, ciliary body, choroid, sclera, and the optic nerve, with x-ray visualizations of the probable involvement of the hypophysis and the structures in the middle fossa of the skull

Oxycephaly

Diagnosis—A case of oxycephaly characterized by exophthalmos, an abruptly rising forehead and a dome-like prominence at the anterior fontanelle has been described by D B Davis and J. C. King. 64 To exclude the presence of oxycephaly, they advocate roentgenographic studies in all cases of unexplained exophthalmos associated with deformity of the skull or with divergent strabismus

Perimetry

Pregnancy-After reviewing the literature on chiasmal syndromes occurring in pregnancy, A Hagedoorn⁶⁵ adds one case from his own experience which at autopsy revealed a suprasellar meningioma When the patient was first examined, she presented normal peripheral fields and unilateral retrobulbar neuritis with a central scotoma which disappeared after delivery Later, when the patient returned to the physician's office, she was pregnant Defects in the field of vision which definitely indicated a suprasellar lesion were present Hagedoorn recommends careful and repeated examination of the peripheral fields of vision in cases of pregnancy which are complicated by retrobulbar neuritis in order to exclude the presence of tumor in the hypophyseal region

Physical Therapy

O. B Nugent⁶⁶ is of the opinion that (1) deeply penetrating short-wave infra-red rays possess a valuable heating effect, (2) visible radiation is of doubtful value, and (3) ultra-violet rays are of benefit in the treatment of ulcerations and necrosis of the epithelium of the cornea and conjunctiva, blepharitis, vernal catarrh and trachoma However, H Gradle⁶⁷ states that ultra-violet therapy is of practically no value

except for cases of herpetic involvement of the cornea

Short-wave — Short-wave therapy was employed in the treatment of 170 patients suffering from inflammatory diseases of the eye ⁶⁸ Approximately 1000 treatments were administered over a period of two years Short-wave treatment was not given to cases of glaucoma, recent retinal detachment, acute purulent conjunctivitis and tuberculous periphlebitis of the retina

Berger concludes that because it penetrates to a greater depth, short-wave therapy is simpler and more effective than diathermy. A 20-minute period of treatment is most desirable. Among the pyogenic conditions which yielded favorable results were serpent ulcer, infected perforating wounds, postoperative inflammatory reactions and deep keratitis. Herpetic diseases and tuberculosis of the eye were also benefited.

Pterygium

Etiology—According to T J Dimitry, 69 dust is not the etiologic factor in the production of pterygrum. His conclusion is based on a statistical survey of the prevalence of pterygra in the various states of the United States of America.

Retina

Embolism of Central Artery in Thrombo-anglitis Obliterans—It has been pointed out that embolism of the central artery of the retina or of its branches may occur as an early symptom of general vascular disease, viz, thrombo-anglitis obliterans 70 This condition was observed in a man, 45 years of age, whose left leg required amputation for gangrene as a complication of thrombo-anglitis obliterans Embolism of the central artery had been noticed four years before the leg was affected

Detachment — Allergy—Lateral detachment of the retina occurred in a girl, 21 years of age, who presented asthma, eczema, and general evidence of allergy since the age of three years 71 Because the skin and the retina are embryologically related, Balyeat suggests that in some cases of detachment of the retina, allergy may be a primary etiologic factor

Cystic Degeneration—It has been observed that central vision is often defective after successful operations for detachment of the retina 72 Reese explains that not only the detached retina in general but also the macular region in particular usually undergoes cystic degeneration

Tears—Location—A means of predicting the probable site of a tear in the detached retina is suggested by Schiff-Wertheimer 7.3. In myopic patients of middle age, the tear is usually located in the upper part of the retina near the vertical meridian. In nonmyopic patients beyond middle age, the tear is situated along the horizontal meridian usually on the temporal side. In young nonmyopic patients and in children, the tear is usually a disinsertion at the ora serrata in the infero-temporal quadrant.

Retinitis Centralis—Central retinitis or chomosetimitis with central scotomas occurred in the left eyes of two stokers 74. The right eye was normal in each case. The lesions in the left eye are attributed to the fact that stokers usually direct the left side of the face toward the fire. He recommends wearing dark glasses to protect the eyes against injury from the heat rays.

Schuller-Christian's Disease

Diagnosis—E R. B Atkinson⁷⁵ describes the clinical and postmortem findings in Schuller-Christian's disease. In addition to the usual findings, namely, osteoporosis, exophthalmos and diabetes

insipidus, the disease may be associated with lipoid granulomas in the cornea, conjunctiva, and fundus, neuritis, papilledema or atrophy of the optic nerve, and crossed diplopia

Sclera

Scleromalacia Perforans - Diagnosis - A case of scleromalacia perforans occurred in a man, 76 years of age 76 The patient had been injured by a chip of wood two years previously A small, red, painful nodule appeared at the insertion of the superior rectus mus-The center of the nodule became necrotic. Following the expression of caseous material, the nodule disappeared. The sclera became so thin that a bluish area could be seen through it Similar nodules appeared and disappeared through the same process until 3/3 of the circumference of the sclera, anterior to the equator, was involved

Scleromalacia; Polyarthritis — F. A Kichle⁷⁷ also reported a case of scleromalacia of both eyes in a woman, 64 years of age, who was affected with arthritis deformans involving practically every joint. The sclera lost its white appearance and became slaty gray, but the cornea, media, and fundi were normal when first examined After several years, cataracts and clouding of the corneas developed Later, multiple radiating perforations and degeneration of both eyes developed so that only light According remained perception Kichle there seems to be a relationship between scleromalacia and polyarthritis

Sympathetic Ophthalmia

Etiology—Rhinogenic—According to B Waldmann⁷⁸ spontaneous serous iritis and sympathetic ophthalmia are identical. He provides international statistics to demonstrate that sympathetic ophthalmia is a seasonal ailment occurring more

commonly between the months of October and April when intranasal disease is more common than between May and September Sympathetic iridocyclitis often begins as an optic neuritis because the optic nerve in the sympathizing eye plays an active part in transferring the disease

Waldmann concludes that the common etiologic organism is present in the nose and the accessory nasal sinuses and that an eye operation, tuberculosis or syphilis lowers the resistance of the uveal tissue to this organism.

Syphilis

Syphilis — Treatment — Tryparsamide-Over a period of 18 months, Max Fine and Hans Barkan⁷⁹ administered 1800 injections of tryparsamide to 132 patients suffering from neurosyphilis. These patients developed permanent reduction in the field of vision (in two of these the routine procedure of checking the fields of vision was not observed until the ninth injection), three presented reduced visual acuity, six developed only subjective symptoms, eight disturbed fields of vision, five impairment of the field of vision which recovered completely after discontinuance of tryparsamide for a period of a month or two.

Glare, blurring, dazzling, smokiness, appearance of corrugation or heat wave shimmering, a bright object passing before the eye, are subjective indications that the field of vision should be examined Objective changes do not appear in the fundus until three to six weeks after serious loss of visual acuity or of the field of vision. Central vision is usually preserved until marked constriction of the field of vision has developed

Fine and Barkan recommend testing the vision and examining the fundi and fields before the first, third, fifth and tenth injection, and before every subsequent tenth injection They concede that tryparsamide therapy in neurosyphilis is hazardous particularly in those cases which present optic atrophy However, this danger can be greatly reduced by having routine examinations of the fields of vision, fundi, and visual acuity by an ophthalmologist The value of tryparsamide as a therapeutic agent for syphilis justifies its use

Uveitis

Paracentesis after Typhoid Vaccine—A L Brown⁸⁰ recommends paracentesis of the anterior chamber after intravenous administration of typhoid vaccine as an additional therapeutic measure in the treatment of nonspecific, acute uveitis He advocates from 20 to 25 million typhoid "H" antigen (a compound of the vaccine) intravenously repeated every 36 to 48 hours Paracentesis of the anterior chamber was found more effective if 15 million typhoid "H" antigen injections were repeated at 48hour intervals

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OTORHINOLARYNGOLOGY

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OTOLOGY

By Francis L Lederer, M D

EXTERNAL EAR

Streptococcic Dermatitis

Itching and scaling dermatoses have been found to be of streptococcic origin in some instances by J H Mitchell¹ who presents ten case reports in which this was the causative factor. He does not consider streptococci of the skin to Pruritic and scaling be saprophytic dermatoses of the ears are frequently encountered by both the aurist and the Various terms, such as dermatologist "eczema" and "seborrheic dermatitis," are applied to them Retroauricular intertrigos, with serous crusting, scaling and fissuring, are not infrequently seen and are recognized by many as due to a streptococcus

The clinical manifestations of postaunicular intertrigo are fairly definite. The lesions of the concha may or may not be preceded by 'running ears'. The patient gives a history of gradual onset of itching in the canals, which in time may become very troublesome. One of both ears may be affected but again, as with the postauricular lesions, the activity is rarely bilaterally symmetrical

The diagnosis must be verified by laboratory methods adapted to the purpose Microscopic demonstration of the streptococci in the serum from the fissures and in the squamelike crusts is not at all difficult

Otomycosis

In summarizing their report on effective fungicidal agents in the treatment (810)

of otomycosis R McBurney and H B Searcy² state

- 1 The fungicidal effect of 69 substances, alone or in combination, has been compared *in vitro* and in a number of instances *in vivo*
- 2 Similarly the bactericidal effect of 38 of these substances has been studied and compared with the fungicidal
- 3 As a result of these studies a system and formulae for effective treatment of otomycosis are set forth
- 4 Exclusive of 24 combinations giving negative results, an average of the effectiveness of 11 combinations containing two per cent thymol similarly compared with 27 containing no thymol showed that the thymol combinations are 2.5 times more effective against aspergilli and 1.5 times more effective against staphylococci. Thymol combinations alone were one plus times more effective against aspergilli than against staphylococci.

In conclusion Many of the so-called fungicidal substances used in the past and introduced for present use as such have no effect upon aspergilli. This is particularly true with alcohol in all dilutions. The fungicidal effect of any effective substance is relatively the same for various species of aspergilli. Therefore the fungicide of choice will have a similar action on all species of aspergilli found in the ear. Thymol, two per cent, in 70 to 95 per cent alcohol or combinations of thymol in alcohol, used with well established germicides, have proven

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to be most effective fungicides against aspergilli, as shown in vitro and in the treatment of some 150 cases of otomycosis The use of two per cent thymol in alcohol or in combination with effective germicides is more effective against aspergilli than non-thymol combinations. The effective fungicides studied are likewise good germicides where staphylococci accompany otomycosis selection of any substance or combination for use in treatment on a basis of fungicidal or germicidal action or both, it is felt that substances having a phenol ratio less than one are of little value The value of the time honored use of alcohol and of alcohol containing two per cent salicylic acid lies in the solvent and drying action of the former and in the exfoliation produced by the latter rather than in fungicidal-germicidal action Of the substances used in combination with two per cent thymol in alcohol, cresatin, merthiolate solution, No 45 (1 1000), and thymol-boric-iodine mixture have yielded the best results

Total Reconstruction of the External Ear

This is discussed by J. K. Nattinger³ who presented cases in which the basic principle involved is that of providing the new ear with a support that is fundamentally fitted for this purpose. Ear cartilage is the ideal graft in that it is already of a proper shape and size. It is thin, it grafts easily, and seemingly bears intrinsic properties that prevent its absorption.

It has been found that a graft of this type will maintain its size and shape perfectly in the mastoid location, while frequently the same cartilage implanted beneath the skin of the chest wall or elsewhere will be absorbed within a few weeks

Once the graft is obtained, the steps required to implant it and its subsequent swinging into position are a matter of almost routine technic. The vital part of the entire procedure is to have all the steps of the operation definitely mapped out so that when the graft is finally swung into place it will remain without tension.

Frequently this type of graft can be used where there is a substantial rudimentary ear remaining. Such remnants may be used after the major grafting to provide the helix and helix minor, which obviates the necessity of making a tube flap for these parts. Bits of buried cartilage may be moved about beneath the skin to form a tragus.

In the event that there is no external auditory meatus, the canal may be constructed first and the graft so placed that when it is swung forward it will lie directly over the opening

The razor grafted area over the mastoid region may again be available for use as a flap after a period of six weeks if further material is necessary

MIDDLE EAR

Sound Localization

A series of 20 experiments performed by E G Wever and C W Bray⁴ on guinea pigs dealt with the effects of sodium chloride upon the electrical responses of the cochlea. The magnitude of responses was determined in absolute units for stimulating tones of known intensity, both before and after the application of sodium chloride. In most of the experiments the substance was applied to the round window membrane, in certain others it was applied through an opening at the apex of the cochlea.

Results are given to show the course of changes in the responses for different

frequencies subsequent to the application of sodium chloride. A study of functional relations between intensity of stimulation and magnitude of responses showed little alteration in form or slope of functions for high tones, and slight reductions of slope for low tones. Concurrent observations from round window and apex showed a difference in the effects of sodium chloride, as recorded from the two positions, the impairment of response was greater from the electrode in the region where the substance was applied. Several processes are suggested in explanation of the results

Three features of the action of sodium chloride are discussed in relation to the problem of cochlear localization. These are the low degree of specificity as regards stimulus frequency, the differences in the observations at base and apex of the cochlea, and the greater reduction in slope of the intensity functions for low than for high tones. It is suggested that these facts indicate broad rather than specific localization of tones in the cochlea.

Middle Ear Disease

Chronic Suppurative Otitis Media—One of the most difficult problems to contend with is the treatment of chronic suppurative otitis media, according to C H Christoph⁵ who recommends an iodine-boric powder Christoph employs the following routine

- 1 A careful examination of the nose and throat for deflected septa, sinus disease, infected tonsils, pharyngitis or adenoids
- 2 A routine hearing test with the audiometer and tuning forks. This should be repeated at intervals
- 3 In case of vertigo, nystagmus and other symptoms of labyrinthine irritation, the caloric and Barany rotation tests

- 4 A general examination by an internist
- 5 Examination of the drum for location of perforation, presence of polypi or granulations
- 6. Bacteriologic study of the secretion
 - 7 Wassermann and tuberculin tests
 - 8 X-rays of sinuses and mastoid

When abnormal conditions are found in the nose or throat these are taken care of by treatment or *surgery*. The eustachian tube is *inflated* and the patient's general condition supported by *tonic* and *hygienic care*. If no polypi or granulations are present the *iodine powder* is blown in, after the ear is thoroughly cleansed

If the ear remains dry, the patient is instructed to leave it alone between visits. If it becomes moist he cleans it with cotton and instills a few drops of boroalcohol (saturated solution). No irrigation or water in the ear is permitted. Those showing symptoms of cholesteatoma, labyrinthitis, facial paralysis or intracranial complications were considered operative. A chronic running ear is not in itself an indication for a radical mastoid operation. The patient cannot be given the assurance that the ear will become dry, the radical is employed as a life saving measure.

In considering the treatment of chronic discharging ears in children, C S Beney⁶ finds that cases may be divided into four groups according to the clinical picture observed

I Treatment should be conservative in those cases in which there has been a discharge from three to six months, or more, with a central perforation, which will not heal, where the discharge is not offensive or profuse and hearing is not particularly impaired. The perforation may be enlarged, the ear cleansed, followed by cauterization of the edges of the

perforation either with silver nitrate or trichloracetic acid. This will often be followed by a cure and cessation of discharge. Should the condition continue, conservative treatment may be continued.

2 In cases where there is a large central perforation with polypi or excessive granulation tissue, the perforation is unlikely to heal "Polypi or granulation tissue must first of all be removed, followed by routine treatment of cleanliness and insufflation of powder If after this there is still a slight discharge which is not offensive, and the hearing has improved, we may be well content, as probably this very slight mucoid discharge is coming from healthy granulation tissue of the mucosa lining the tympanic cavity If the discharge is more profuse (in spite of inoffensive character), it is probably coming from the mastoid antrum, polypi will recur, and it is justifiable to obliterate the mastoid antrum by a conservative operation

3 In cases where the perforation in the drumhead is marginal and in many cases multiple, bony necrosis is nearly always present, usually some part of the tympanic ring, and in most some necrosis of the malleus and incus will be found, the incus being frequently attacked owing to its poor blood supply and its close relation to the aditus and antrum Local treatment with caustics, such as silver nitrate, etc, may cure in some few cases, but it is wiser to explore and deal with the condition by operation

4 In these cases every few weeks or months there is recurrence of pain and possibly temperature, the hearing diminishes and slight attacks of giddiness are complained of Pain comes on with partial cessation of the discharge and is relieved only when there is a free flow of pus from the ear. These cases are

really dangerous and lead sooner or later to intracranial complications.

Apart from these four types there are those similar to the last where the only symptoms are general ill-health with some slight attacks of giddiness or nausea and slight offensive discharge Cholesteatoma may be found upon operation. Cleanliness should be the watchword in dealing with this condition.

VERTIGO

Vertigo as a symptom of vascular diseases is discussed by S L. Shapiro7 who feels that any discussion of vertigo must be based on a clear conception of what is meant by the term. One might begin by defining it as an apparent displacement experienced by an individual in relation to his surroundings. Such a definition would recognize movement as the first essential of vertigo. The patient may feel as if he is turning around or as if the room is revolving about him (rotational vertigo), the floor or ceiling may appear to tilt toward him or to feel like the deck of a ship at sea instead of firm ground (tactile error), or he may feel a strong pull forward, backwards or to one side (pulsion) The awareness that the experience is false constitutes the second essential, serving to differentiate vertigo from the ataxias of tabes and similar diseases where the sensation comes after the loss of equilibrium has taken place. A third feature is a strong tendency towards compensatory movements, the person affected will put out a hand, lean against a wall or merely stand still for a moment Add further that the onset is abrupt and the duration of the attacks generally brief and we have all the elements that enter into a description of vertigo

In describing these sensations patients usually use the word, "dizziness" This

term, however, is also employed as a synonym for many unpleasant experiences such as spots before the eyes, things growing black before the eyes, double vision, head noises, nausea and various emotional states It is important not to accept a simple complaint of "dızzıness" without further questioning since, whatever our idea may be as to significance of flashes before the eyes or some of the other symptoms which the patient may really have in mind, there can be no doubt as to the meaning of an attack of true vertigo This indicates a disturbance either in the internal ear or in the pathways leading from the labyrinth to the brain or in the brain itself and as such demands serious attention

The vascular diseases which Shapiro considers in his discussion are vasomotor instability without evidence of structural alteration in the blood vessels, blood disturbances (anemia and leukemia), circulatory disturbances with organic changes in the blood vessels of the internal ear or brain and cardiac abnormalities

The diagnosis involves two factors First, whether or not there is a true vestibulai disturbance, second, the site at which vertigo is produced, ie, whether in the internal ear or in the brain and, if possible, the approximate location in the brain The type of vertigo present, the kind of nystagmus, the presence of ataxic manifestations as past pointing, drift reaction or Romberg and their relation to the slow component of the spontaneous nystagmus, the presence or absence of tinnitus or impaired hearing simultaneously with the vertiginous attacks and the results of the cochlear and vestibular examination between attacks are all necessary to formulate an opinion

The author lists other conditions which cause vertigo

- 1 Within the middle ear
 - (a) Acute or chronic otitis media causing toxic absorption without an obvious lesion of the internal ear
 - (b) Obstruction of the eustachian tube
- 2 Within the internal ear
 - (a) Labyrinthititis, circumscribed, serous or suppurative, after middle ear infection
 - (b) Acute infectious diseases without middle ear infection
 - (c) Lues
 - (d) Herpes zoster oticus
- 3 The eighth nerve
 - (a) Neuritis following any infectious disease
 - (b) Neurofibroma
- 4 Intracranial conditions other than those mentioned
 - (a) Meningitis, serous or suppurative
 - (b) Brain abscess
 - (c) Tumors of the posterior fossa
 - (d) Systemic diseases as cerebrospinal lues, encephalitis, multiple sclerosis, etc
- 5 Toxic Vertigo—This includes various foci of infection in the teeth, sinuses, tonsils or other parts of the body and a large group of drugs which irritate the vestibular apparatus, such as alcohol, nicotin or quinin.
- 6 Reflex irritations, such as those from impacted teeth and plugs of cerumen in the external auditory canal have been known to cause vertigo Usually the trigeminal nerve forms a part of the arc but irritation of the carotid sinus itself is also known to produce vertigo or syncope

7 Emotional disturbances

The treatment of vertigo of caidio-vascular origin is essentially that of the cause Drugs such as luminal, bromides, and scopolamin are recommended as sedatives. Between attacks in the functional vasomotor type the patient is studied for signs of abnormal vagus or sympathetic activity. Those with small pupils, dry skin and slow pulse Shapiro recommends atropin, those with large pupils, moist skin, frequent flushing and

rapid pulse on pilocarpin. It is impossible in many cases to state whether the immediate cause of the labyrinthine storm 1s a vascular dilatation or a spasm so that treatment along this line must be empirical. Injections of acetylcholine (01 Gm) relaxes a vascular spasm and adrenalin sometimes terminates an attack indicating that a vasodilatation was at fault In certain cases dehydration with a salt-poor diet and large doses of ammonium chloride gives good results. Caution in advising surgical means of curing vertigo such as the division of the eighth nerve is voiced by the author

Vertigo in Brain Tumors

The observations of E A Spiegel and A Alexander⁸ on brain tumors seem to corroborate the assumption of a representation of the labyrinth in the cerebral cortex, particularly in the temporal lobe Parts of the frontal lobe, especially the centro-opercular region, must also be taken into consideration as a place at which vestibular and spinal impulses joined in the subcortex (cerebellumruber system) may enter The conception that vertigo in brain tumors is only a general symptom of increased intracranial pressure seems to need a revision

Intoxication caused by nasopharyngitis as an etiologic factor in toxic labyrinthitis is proposed by T P O'Connor 9 Twenty-three cases have been studied which displayed the typical symptoms of true labyrinthine disturbance. In none of these patients could local lesions of the labyrinth, brain, middle ear or mastoid be demonstrated, syphilis and poisoning were conclusively ruled out search for a focus of infection in every case revealed, in the absence of all other significant physical changes, active subacute or chronic nasopharyngitis inflammatory nature of the condition was confirmed by cultures of the nasopharynx

in all cases, most of which produced a heavy growth of streptococcus viridans. Treatment of the nasopharyngeal vault was followed by prompt relief of symptoms

W. E. Dandy¹⁰ claims to have shown that Méniéres disease and pseudo-Méniére's disease could be cured by section of the auditory nerve or equally well of the vestibular branch alone. His series of operations has now reached 170 in 160 patients, ten being bilateral. There has been no death, and except for four early facial palsies, no after-effects in the unilateral cases. According to the author there are few diseases so easily diagnosed and so perfectly curable. The absence of necropsy material throws the burden of pathologic disclosures on conditions found at operation.

In not a few case records of acoustic tumors one can find a story of perfectly characteristic Méniére's attacks. The reason for the general erroneous belief that dizzy attacks are uncommon with acoustic tumors can be explained by the fact that dizziness is but a minor part in a group of severe signs and symptoms that are usually adequate enough to make the diagnosis A series of five large arterial loops (from the anterior inferior cerebellar artery) in the lateral cistern are, the author believes, equally positive lesions in the production of Méniére's disease

The intracranial section of the auditory nerve for treating vertigo is employed by M Ombrédanne, 11 who utilizes Dandy's method in a modified form partial section of the auditory nerve, which suppresses vertigo and pain but saves the sense of hearing Of 19 cases of simple Méniére's syndrome in which operation was performed, all were successful Of 17 patients with atypical Méniére's syndrome, 14 were cured, two died and in one the symptoms persisted

Some of these patients were very vertiginous, were deaf in one ear, and had an intolerable tinnitus. The two deceased were chronic otorrheic patients who previously had several operations

DEAFNESS

The problems of the deaf have been studied by T L. Tolan¹² with particular reference to those who are so far handicapped as to find hearing a distinct effort and therefore, includes those who find it difficult to be instructed by means of the There are many classifications as to the types of deafness, but the most comprehensive divisions are those of a deafness which is either congenital or acquired Thorough family history of the patient is of extreme importance Endocrine history sometimes throws some interesting and helpful light on the etiology and prognosis of the condition Throughout our whole relation with a person with impairment in hearing, we must remember that this condition is connected with the individual as a whole and not just isolated pathology

After the type of impairment has been determined, we are in a position to treat those patients who are capable of being instructed by ear In the so-called totally deaf child the importance of a caloric test is stressed, as it is estimated that 30 per cent of the congenitally deaf have residual hearing In these children especially a great deal can be done to stimulate the nerve to better hearing and also more effective instruction Until recently there has been controversy over the relative value of treating the deaf The three systems which have been employed are (1) The sign method, (2) the oral method, (3) a combination of these two At the present time, however, the sign method has been almost entirely discarded and instruction is entirely by the

oral method In people who have learned to talk previous to their impairment, the problem is, of course, a different one Having mentioned the most important treatment in these patients (oral and lip reading), it is very often necessary to further relieve the impairment by the use of mechanical devices Another method of treatment which has been stressed the last few years has been the vibratory and sound machines If the impairment cannot be helped, the patient should be tactfully apprised of his condition and readjusted A great deal of help can be had from the League for the Hard-of-Hearing

The early detection and treatment of defective hearing in children is stressed by H Newhart 13 The magnitude of the problem is indicated by the statement that 10,000,000 persons in the United States have a demonstrable deficiency of hearing, causing a recognized or potential handicap Of these 3,000,000 are school children, of whom 300,000 already are handicapped in their scholastic achievement Newhart proposes that an accurate periodic testing of the hearing by modern scientifically approved methods is necessary for the early discovery, diagnosis and successful treatment of many diseases of the ear which result in impairment of hearing The incorporation in the school health program of the regular periodic testing of hearing of all school children has proved to be the most effective single procedure for reducing the incidence of loss of hearing

It is estimated that there are about 40,000 persons deaf since infancy in Great Britain ¹⁴ Nearly 4000 children of school age in England are deaf enough to require education in special schools Of these, 500 in the schools of London were the object of the study, the results of which constitute this report. The report shows that nearly one-half of these

children were born deaf, others become deaf on account of diseases that might be preventable. The majority of the children investigated were afflicted with a hearing defect before the age of two vears All gave evidence of some degree Because of the extreme of mutism vouth of those examined, the author overcame many obstacles in attempting to obtain an accurate estimate of the hearing loss presented by the children There were experimental studies made with amplified sound which demonstrated not so much an improved faculty for hearing, as it resulted in improvement in speech of these afflicted children Hence the use of amplified sounds is recommended to improve speech among such patients The reports will interest otologists because of the comparisons made of the results of hearing tests, new and old.

G Selfridge¹⁵ declares that the work of Peters of Oxford proves conclusively that some factor in the vitamin B complex is necessary for perfect biologic Thus the oxidative reduceauilibrium tion system is necessary in order to prevent the accumulation of lactic acid in certain parts of the brain The finding of a definite demyelinization in both branches of the eighth nerve in a series of rats and chicks on a diet deficient in the different factors of the vitamin B complex B1B2 and especially filtrate factors B6B7 or K1K2 as shown in Covell's histopathologic studies, warrants the assertion that the lack of sufficient vitamin B in the human diet is probably the principal cause of the degeneration found in the eighth nerve The clinical use of B₁ parentally, B₁B₂ absorbate, and particularly the rice bran B complex, appears to be the cause of the improved hearing noted in the audiograms of clinical cases Large doses of carotene (30,000 units daily) over a period of months have caused no further change in hearing as demonstrated by the audiograms. Perhaps if the dosage of carotene or vitamin A was carried on over a longer period under the control of the photometer, further changes might be noted. The use of thyroid, except possibly in rare cases, does not influence the nerve changes. Cody's finding of a whitish edema in his animals on a vitamin B deficiency diet, and as seen in human beings with the pharyngoscope, appears to be somewhat conclusive as to vitamin B deficiency

The use of hearing aids is ably presented by A W G Ewing, I R Ewing and T S. Littler 16 Improvements in the field of broadcasting have been carried over into the field of otology, so that by means of sound-amplifying apparatus many of the deafened have been The authors tested their deaf subjects in a number of ways and arrived at several interesting conclusions testing patients by a series of pure tones obtained from an audiometer, they found that a reliable index of the intelligibility of speech to the deaf could be obtained They satisfied themselves that hearing aids are not, as many deafened persons believe, harmful to the user and do not cause further deterioration of the hearing They emphasize the necessity of standardizing tests for the intelligibility of amplified speech and suggest that this is best done by means of an amplifier system properly constructed They admit that impairment of hearing of certain types cannot at present be improved even with the best apparatus available and that hearing aids are still a disappointment to the patient and the physician

SYPHILIS OF THE INNER EAR

In over three per cent of all luetic persons according to the statistics of Oskar

Beck and Kerl, syphilis of the inner ear is present in the sixth to eighth week after infection Claus¹⁷ describes the following cochlear symptoms. a positive Rinne, marked shortening of the head bone conduction even with normal hearing (according to V. Urbantschitsch in 80 per cent of all luetics!) and independent of the Wassermann reaction, that is, even after successful treatment According to Wanner, the diagnosis of lues is almost certain when a tuning fork is not heard from the crown of the head Then there are the following vestibular symptoms. abnormally strong or abnormally weak caloric and turning reactions, with differences between right and left (typically without complaint of the patient) indicating vestibular apparatus dysfunction, or there may be normal or even heightened caloric reaction with almost no turning reaction, and-less typical-also the reverse The symptomless destruction of the vestibular apparatus with normal or subnormal hearing is found almost exclusively with lues According to Gatscher, it is due to changes in the region of the eye muscle nuclei Herxheimer reaction has become very rare since the general use of aisphenanine combined with mercury or bismuth Inner ear deafness with marked shortening of the head bone conduction may be an early symptom of tabes congenital lues, the ear symptoms usually appear between the eighth and the twentieth years A complete Hutchinson triad is rare

TINNITIS AURIUM

The treatment of tinnitus aurium by the *intravenous use of local anesthetic agents* was studied by R B Lewy¹⁸ who contends that since there are so many etiologic factors in the production of tinnitus, and despite this procaine hydrochloride has some effect in varying

its intensity in many types, it is assumed that its action is central Lewy feels that procaine hydrochloride and nupercaine in proper doses are safe drugs to use in the treatment of tinnitus by intravenous injection He also regards procaine hydrochloride as effective in reducing the intensity of tinnitus (continuous) in the large majority of cases associated with: (a) Normal hearing, (b) deafness of the inner ear (only two failures), (c) otosclerosis, and (d) mixed deafness Lewy found that quinine and ethyl carbamate produce too severe a reaction to be used intravenously in the treatment Pulsating tinnitus is not of tinnitus relieved by this method of treatment Its effectiveness is determined only by experiment

Data on the acuity of hearing by bone conduction for 516 patients with a conductive type of impairment (acuity by bone conduction being better than that by air conduction) are presented by A Ciocco 19 The data have been statistically analyzed to determine whether or not the acuity of hearing by bone conduction is related in any way to age, the condition of the tympanic membrane, tinnitus, a history of familial deafness and the degree of impairment of hearing by air conduction Prolonged bone conduction time was found in 267 per cent of the cases, normal bone conduction time in 661 per cent and shortened bone conduction time in 72 per Those with prolonged bone conduction time were, on the average, the youngest, those with shortened bone conduction time were the oldest the average, the acuity of hearing by air conduction of persons with prolonged and with normal bone conduction time was similar and was more acute than in patients with shortened bone conduction A normal tympanic membrane was observed with greater relative fre-

quency in persons with prolonged bone conduction time The incidence of tinnitus was practically the same for all groups The incidence of a family history of deafness was highest in those with prolonged bone conduction time and lowest in those with shortened bone conduction time The differences are statistically significant The effect of age on the acusty of hearing by bone conduction appears to be the most noteworthy finding. Prolonged bone conduction time in all probability represents the upper "tail" of the frequency distribution of the normal variation The fact that the persons with such bone conduction were the youngest, on the average, may be regarded as confirming the hypothesis that acuity of hearing by bone conduction is associated with some factor or factors other than the condition of cochlear nerve and end organ

The treatment of chronic catarrhal deafness by the use of x-rays is discussed by F W O'Brien 20 From 1929 to 1935 inclusive O'Brien treated 140 patients by roentgen irradiation, 73 were improved as to hearing and tinnitus, the condition in 65 was unchanged and it was made worse in two Of the improved group, 67 had nine treatments to each ear and six received only eight tieatments, nine treatments have been designated as the acceptable course or cycle Accepting a cycle of nine treatments as the optimum, approximately 78 per cent who received it were benefited No patient has been followed less than a year, the majority for more than three years and some as long as five The much abused tonsil did not seem to play a direct part in the beneficial outcome of irradiation of these cases The x-ray factors employed were 145 kilovolts, 5 milliamperes, 025 mm of copper and 1 mm of aluminum filter at a distance of 50 cm over a field 15

by 15 cm., the exposure lasted five minutes, about 90 roentgens in air being given to each ear-field at one sitting and repeated at weekly intervals for nine treatments. A large field with the hypotenuse of the two right angles extending from the nares to the mastoid tip was chosen deliberately to include the nasopharynx, the course of the eustachian tube and the mastoid and ear structures because of the accepted relationship of lymphadenoid tissue and infection to chronic catarrhal deafness, and, at the same time, to include the origin and distribution of eighth nerve and its communications in the temporal bone for possible neural stimulation

FLIGHT AND THE MIDDLE EAR

Since aviation has attained its present status in travel and warfare, a new field in medicine has had its birth. According to H G Armstrong and J W Heim²¹ airplane pilots suffer more frequently from disturbances of the middle ear than from all other occupational diseases combined

These same writers assume that the deleterious effects of flight on the middle ear depend entirely on the peculiar structure and functioning of the eustachian The rates and degrees of atmospheric pressure changes during flight depend on the rates and degrees of ascent or descent, and these factors become important when it is remembered that the ear is a closed, air-filled cavity with pressure equalization possible only when the eustachian tube is opened Studies were carried on to determine the physiology of the eustachian tubes under marked variations of atmospheric pressure, since the results of such investigation had never been previously reported

Without doubt, although the etiology and symptomatology are of interest, the most practical phase relates to treatment The authors believe that the most useful prophylactic measures in all cases is proper instruction of the individual concerned As long as the patency of the eustachian tube is under voluntary control there is no reason why any person in command of his faculties need experience difficulty at any rate of ascent or descent possible in present commercial aircraft A simple explanation of the functioning of the eustachian tube followed by instructions as to how to ventilate the tympanum, when to ventilate it and how frequently this is necessarv should suffice

Active treatment consists first of relief of pain in acute cases Politzerization is valuable if the drum indicates the existence of either positive or negative pressure Heat is an effective measure The method of choice consists of filling the external auditory canal with quantities of water at from 110° to 115° F (433° to 455° C), followed by prolonged application of dry heat Proper attention to the nose and pharynx and suitable aftertherapy in the form of dry heat to the ear are other important procedures in the program. In chronic aerootitis media, stenosis of the eustachian tube should be looked for and treatment directed to its relief

COMPLICATIONS OF OTITIS MEDIA

A A McConnell²² classified intracranial complications of otitis media as suppurative and nonsuppurative Nonsuppurative complications are of two kinds, one an encephalitic lesion which gives rise to both local and general symptoms and the other a derangement of the amount or of the circulation of the

cerebrospinal fluid, resulting in the accumulation of the fluid and a rise in the general intracranial pressure. When symptoms and signs of increased intracranial pressure develop in the course of otitis media and clinical methods fail to establish a definite diagnosis, ventricular puncture is safer and more informative than lumbar puncture and should be used first. If a communicating hydrocephalus is found, *lumbar puncture* may then be used for treatment.

Petrositis

This year's Congress of German Otorhinolaryngologists met at Cassel The main topic was "Suppurations of the Pyramidal Cells" Prof Otto Mayer²⁸ of Vienna delivered the principal lecture In recent years, he said, scientists of all lands have given more consideration to suppurations of the pyramidal cells These disturbances, it has been determined, can be responsible for many intracranial complications. In some cases as a thoroughgoing removal of the mastoid cells (mastoidectomy), the surgeon believes that the focus of infection has been completely done away with until he is confronted with a manifestation of these sequels In cases that terminated fatally despite a carefully performed operation, microscopic post-mortem examination of the pars petrosa of the temporal bone disclosed foci of inflammation in the areas anterior to the semicircular canal, and because of the location of these foci they had not come within the scope of the intervention A study of pyramidal cell suppuration is of especial importance, as most of the present day fatal cases of meningitis following acute otitis media are based on purulent foci in the pars petrosa The pyramidal apex syndrome as a clinical sign of the disorder was established by Gradenigo in 1904

The following should be kept in mind with respect to pyramid cell suppuration It may form a circumscribed focus. spread over the entire surface of the labyrinth or lead to an abscess, which may be either closed and hence incapable of discharging into the spaces of the middle ear or open to the extent that some influx of pus into the middle ear is possible. Abscesses may also occur in various cell tracks and finally, pyramidal cell infection may assume the character of a proliferating inflammation and run its course without much suppuration But if the suppurative process is sufficiently active it can perforate the posterior or middle cranial fossa, the labyrinth, the carotid canal, the foramen lecerum posterius or the pharynx It is essentially a more favorable sign if perforation takes place in the last named region, forming a retropharyngeal abscess X-ray visualization is a valuable diagnostic aid Operative treatment is usually indicated Cases that come early to diagnosis are treated conservatively (by paracentesis), since in these the prognosis is favorable Even cases in which the suppuration is of long standing may be cured, mastoidectomy with a thoroughgoing extirpation of the cells and, above all, those proximate to the labyrinth is here indicated If suppuration persists, radical operation should follow Only if the foregoing safe and tried procedures fail to produce results should one look for a focus in the apexes

Professor Zange of Jena has found that pyramid cell suppuration and related processes which appear in the region of the inner ear, in the pars petrosa or in the adjacent meningeal spaces are capable of involving numerous other cerebral nerves. Most prominent among these nervous diseases are labyrinthine-vestibular disorders, namely disturbances of the equilibrium, which, because of their

peculiar character and the preservation of peripheral irritability of the labyrinth, can today be with certitude distinguished from labyrinthine inflammations

Some other data of interest were contributed in the discussion. Report was made of the healing of a pyramidal abscess that had erupted spontaneously into the sphenoidal sinus. Similar conditions may also heal spontaneously, especially in child patients. But, on the other hand, there are the hopeless cases, especially the rapidly advancing osteomyelitis. The latter are particularly apt to prove fatal if combined with the otitis of nurslings.

Deep otogenic inflammation of temporal bone (petrositis) is presented by R. Lund,²⁴ who discusses simple petrositis and osteitis of the petrous portion of the temporal bone on the basis of 54 cases comprising 38 cases of acute or subacute suppuration of the middle ear, 13 of simple chronic and three of cholesteatomatous suppuration In the 54 cases, 89 foci were emptied, 15 anterior and 74 posterior, the greater number of interventions on the posterior foci being partly due to their easier accessibility The main symptom in deep osteitis is pain, differing in character and location from the usual ear pain. It is generally neuralgic, most often violent. The most common localization is one or more of the fields of the trigeminal branches In 13 cases in children under the age of ten years, there was no definite statement as to pain In part of the second group of 24 adults, there was pain, sometimes violent, but indefinite In the third group of 19 patients, typical petrositis pain was established, 14 of these had acute suppuration of the middle ear, the typical pain appearing in 11 during the first days of the suppuration and in three on the seventeenth, the thirteenth and the fortyfirst day, respectively These pains cease spontaneously or after the operation on the ear, permanently in many cases, in others they recur. When the field of all three trigeminal branches is affected, the presence of a disturbance of the gasserian ganglion is likely, it is certain if disturbances in sensitivity are established also in the trigeminal fields. The neuralgic pain in the orbits, emphasized in the literature, occurred in only four cases, in two of which the apex was affected In three cases there was no orbital pain in spite of total petrositis In emptying focus VI, especially when the osteitis continues into focus III. which is frequent, the facial nerve is sometimes laid bare above the styloid foramen, usually, without lesion of the nerve, causing a postoperative paralysis of the facial nerve as seen in six cases The prognosis is favorable In 19 cases there was pronounced disorder of the labyrinth, with complete destruction of the labyrinth in seven and fistulous breaking through the labyrinth in two In case of labyrinthine disturbance during the course of suppuration of the ear, every effort should be made to determine whether or not petrositis is present. If apicitis is not diagnosed before paralysis of the abducent nerve is manifest, the case will often be one of marked meningitis Petrositis in the early course of suppuration of the middle ear, without actual osteitis, has a tendency to spontaneous recovery Even at a later stage, when there is true osteitis in the temporal bone, i e, from the third to sixth week, when operation on the mastoid process is indicated, the prognosis is good without deep intervention. In the subacute stages of the osteitis the disorder is so variable in localization and extent that the prognosis is uncertain In the first stage of acute petrositis, paracentesis often results in recovery

A case of neuralgia of the glossopharvngeal nerve giving rise to symptoms in the pharynx is reported by H. P. Schugt 25 The pain cleared up almost immediately on drainage of an abscess of the petrous tip. Instances of simultaneous disturbance of the glossopharvngeal, vagus and spinal accessory nerves. known as Vernet's syndrome, are cited The syndrome may result from fracture of the skull, tumor of the brain, syphilitic meningitis, abscess or tumor of the petrous tip, thrombosis of the bulb of the jugular vein or any inflammatory process in the region of the jugular foramen. Involvement of obscure etiology in the soft palate, the vocal cords or the sternomastoid or the trapezius muscle may therefore be found to originate in trauma or disease of the area adjacent to the jugular foramen or in a pathologic condition of the petrous tip

J Lempert²⁶ endeavors to establish the rationale of his new technic for apicectomy published in 1936. The various conditions which may result from suppuration within the petrous pyramid are described. The treatment of apicitis is likewise reviewed and the technic for apicectomy quoted from the author's original report. The following conclusions are made.

A new description and a nomenclature of the petrous portion of the temporal bone which conforms to the present day surgical requirements are suggested

Suppurative apicitis *per se* is an indication for immediate surgical intervention on the petrous pyramid, as suppurative mastoiditis *per se* is an indication for immediate operation on the mastoid process

A new technic is described for the surgical treatment of suppurative apicitis and its complications. The complete apicectomy presents the following advantages

- 1. It permits a thorough removal of all diseased tissue within the entire apical carotid portion of the petrous pyramid, while the apicectomy provides for puncture and drainage only.
- 2. It permits a thorough inspection of the posterior surface of the apical carotid portion of the pars petrosa, which heretofore has been impossible
- 3 It permits complete exposure and inspection of the dura in the posterior cranial fossa anterior to the internal auditory meatus.
- 4 It permits inspection of the entire dura of the middle cranial fossa in apposition with the anterosuperior petrosal surface without danger of trauma to the dura proper.
- 5 Through the exposure afforded by this technic, an epidural abscess in the posterior fossa anterior to the internal auditory meatus can be adequately drained
- 6 A collection of pus which has ruptured through the inferior surface of the apical carotid portion can also be drained. The inner table of the inferior skull base surface of the apical carotid portion can be inspected and surgically treated.
- 7 It will expose and drain a pericarotid collection of pus within the carotid canal

The exposure of the internal carotid artery throughout its entire course in the bony canal is to be viewed as an advantage in guiding one safely through the entire apical carotid portion of the petrous pyramid. The internal carotid artery, because of its unvarying course, is a great natural landmark which leads from the end of the basal labyrinthine portion through the entire apical carotid portion directly to the geometric apex of the petrous pyramid and keeps one constantly in the safety zone. It is therefore almost impossible to injure it

The facial nerve and the promontory are never in danger of injury during an apicectomy, because they both occupy an anatomic position posterior to the field of surgical instrumentation.

In all cases of otitic bacterial leptomeningitis, wherein all possible foci within the temporal bone should be removed, this procedure is suggested for the exploration of a possible hidden focus of infection within the apical carotid portion or in the regions surrounding it, which may be the inciting cause of the meningeal infection

The complete apicectomy is suggested as a means of approach to the dura of the posterior fossa for surgical drainage of the cisterna interpeduncularis (supratentorial) and of the cisterna ponti (infratentorial) in the treatment of acute bacterial suppurative meningitis. Such drainage, if instituted early in the disease before the pathologic process envelops the whole surface of the brain, may prove beneficial in the treatment of meningitis.

The surgical treatment of thrombosis of the inferior petrosal sinus may be attempted through this route A complete apicectomy can be carried out when necessary in any type of petrous pyramid, pneumatic, diploic or sclerotic Suppurative apicitis can occur in any type of petrous pyramid No apicectomy is complete or can be completed without exploration of the internal carotid canal, just as no mastoidectomy is complete or can be completed without a complete exploration of the lateral sinus plate No surgical intervention on the apical carotid portion of the petrous pyramid is adequate unless it includes the exploration and inspection of the basal labyrintline portion of the petrous pyramid

All surgical procedures attempted for the relief of suppurative apicitis must necessarily include a *mastoidotympanectomy* (radical mastoidectomy) to be adequate Only through a complete exenteration of the apical carotid portion of the petrous pyramid will the best results be obtained in suppurative apicitis. The complete apicectomy should therefore replace the apicotomy

Petrositis is not often recognized, according to S J Kopetzky,27 who feels that many petrosal infections heal spontaneously Others progress with sudden cessation of aural discharge, occurrence of persistent pain and meningeal irritation The x-ray and clinical picture are important in diagnosis The clinical picture includes as cardinal features appearance of the aural discharge after a period of cessation or its uninterrupted continuance after the performance of a complete simple mastoidectomy, periodic appearance of sensations of pain from branches of the first branch of the fifth cranial nerve, increasing in severity and intensity with decreasing periods of intermission until it is a continuous symptom, low grade fever and increasing general malaise, occasional transient inflammatory or irritative reactions from the living and functioning labyrinth, and occasionally signs of involvement of other cranial nerves—the sixth, the ninth, the tenth and sometimes the seventh An endeavor should be made to recognize the lesion while it is still intrapetrosal Therefore, differentiation must be made between a progressive lesion and one in which recession is taking place

Kopetzky points out that in the diagnosis of petrositis, along with the clinical picture, the x-ray is important, the condition shown on the film varying from halisteresis of the pars petrosa to complete loss of evidence of bone structure

The author states concerning treatment. The first significant fact in need of recognition is that lesions in this area vary considerably with each case "Surgical operation on the petrosal pyramid

should be limited as much in extent as the situation of the lesion permits. No one advocated procedure is applicable to all types of involvement and to all the varying lesions which may be presented in the pars petrosa." The various types of operations indicated for the different localizations of infection are ably discussed by this authority

Kopetzky and Almour treated 46 cases of proved purulent infection in the petrosal pyramid Posterior labyrinthine fistula was present in ten cases and anterior labyrinthine fistula in 21 cases In four cases anterior and posterior fistulas were present and in seven enclosed empyema of the pars petrosa was noted Eight deaths and 37 cures Result Meningitis was present in 11 cases before operation, four of these patients suc-Simple mastoidectomy with cumbing drainage of fistulas was performed ten times, radical mastoidectomy with drainage of fistulas was performed 25 times Almour technic for enclosed empyema was employed eight times and the Lempert technic three times, the latter resulting in three cures

Not included in this series were cases in which petrositis was suspected, but which did not meet his criteria for diagnosis, or cases in which a symptom complex of petrositis was present, but in which healing occurred without resort to additional surgical treatment. In these cases there was no pathologic proof of petrosal involvement

Meningitus

G H Poirier and B E Levesey²⁸ report a case of streptococcic meningitis in which full recovery occurred. There are about 15 reports in the literature in the last 20 years which concern a total of 94 cases, in 53 of which streptococci were cultured. The authors state in their summary. "In reporting this case we

do not wish to create the impression that mastoid surgery is contraindicated in mastoiditis of otitic origin. We realize that infection may invade through the nasal passages and blood stream, and the meningitis may not be associated with the ear condition present but be only an incident. The line of demarcation is difficult and delicate between operative and nonoperative cases and is very hard to define. Each case requires considerable experience and demands not only a clear definite history, but to be backed up with skillful, intelligent clinical findings During the months we are at the infirmary, cases of discharging ears with meningitis are divided into three groups for the purpose of treatment

"The first group comprises cases of meningitis associated with acute disease of the ear of several weeks' duration in which there is clinical and roentgenographic evidence of suppurative mastoiditis. In these cases we do a simple mastoidectomy, bare the dura and expose the lateral sinus

"In the second group, comprising cases of meningitis when chronic suppuration of the ear, with or without acute exacerbation or cholesteatoma, we do a radical mastoidectomy and make a careful search for an extradural abscess or a lead to an abscess of the brain

"The third group, comprising cases of acute fulminating upper respiratory infections with profuse nasal discharge and suppurating ears, of short duration, and meningitis accompanied with no clinical or roentgenographic evidence of destruction in the mastoids, we give symptomatic treatment, general pediatric treatment, lumbar punctures, when signs of intracranial pressure are present, and transfusions when indicated by the blood picture

'Since discharged from the infirmary three months ago, this patient has been perfectly well On careful examination and checkup at this time we were unable to find any physical or mental defect."

George E. Shambaugh, Jr., 29 had a series of five consecutive patients with otitic or nasal sinus meningitis recovered after treatment according to accepted principles These principles consist in the earliest possible diagnosis of meningitis by spinal fluid examination at the first suspicions of meningeal invasion, the cell count being the important A sharp differentiation consideration must be made between localized meningitis, with increased cells but no organisms on smear or culture and with a normal sugar determination, and generalized meningitis, with organisms on smear and culture with diminished or absent spinal fluid sugar As long as the meningitis is localized, treatment should be confined to thorough surgical dramage of the focus in the ear or sinus Occasionally a few organisms may be found on smear but not on culture and here also simple drainage of the suppurative focus may suffice to produce a cure The prognosis of localized meningitis is good if it is promptly recognized and dealt with

Once a generalized meningitis has developed, incision and drainage of the dura at or near the point of entry of the infection may be considered, forced drainage of spinal fluid by the method of Kubie may be employed, the intracarotid administration of antiseptics may be tried, or simple repeated lumbar punctures may be relied on While the prognosis of generalized meningitis of otitic or nasal sinus origin is usually poor, occasional recoveries do occur, especially from meningitis due to the streptococcus

W D Jones³⁰ is forced to the conclusion, after reviewing the literature, that reliable statistics will not corroborate a reduction in the mortality rate in

diffuse purulent meningitis with positive culture of the spinal fluid. However, the rationale of forced drainage combined with serological and chemical therapy and elimination of the original focus of infection may offer some reduction in the near future

Two classifications of meningitis that strike the author as being appropriate in meningitis of otitic origin are First, (a) circumscribed, which may be serous or purulent, (b) serous, which may be circumscribed or diffuse, (c) purulent diffuse meningitis, fulminating type, and second a classification according to bacterial cause Early diagnosis is essential to give the patient the most favorable opportunity to recover, whatever treatments or procedure may be used Having made a definite diagnosis, we should decide on the best plan of treatment in the case at hand and proceed to carry it out, or as near as possible, with the facilities at our command, remembering that we are dealing with a hazardous condition and a most unfavorable prognosis

A review of the literature of the past 20 years discloses an enormous amount of material indicating the many possibilities of the clinical course in cases of septic meningitis of otitic origin when recovery takes place. An additional report of such a case, according to S. A. Sciarretta, 31 is justifiable in view of the fact that recovery is rarely reported after surgical intervention confined to the temporal bone and its adnexa. In the author's case the existence of meningeal infection was proved by the presence of gram-positive diplococci in spinal fluid

The infection was carried into the cranial fossa per continuitatem

The recovery is attributed to the wide surgical exposure of the dura and removal of a portion of the perilabyrinthine cells

The conclusions arrived at by the author are

In spite of the immense amount of laboratory experiments and clinical research by distinguished workers, it will not be denied that the number of instances of recovery from true septic meningitis of otitic origin is comparatively small.

The enormously varied therapeutic methods employed in treating septic meningitis, proves that there is no rational, clearly defined and generally accepted plan of treatment which in any large series of cases can be depended on

Otitic septic meningitis is more common than is generally thought. It would be less frequent if prophylactic measures were more rigidly adhered to by the early and adequate treatment of suppuration of the middle ear

A positive diagnosis of septic meningitis can frequently be ascertained, during its incipient stage, by the judicious use of the various laboratory examinations. It is probable that if the therapeutic measures were employed at an early period more recoveries from septic meningitis could be recorded.

Vaccination against intracranial complications following pneumococcus type III mastoiditis is proposed by J L Goldman and C Herschberger 32 It 1s well known that the presence of this type of pneumococcus in acute mastoiditis offers a serious prognosis because of the frequency with which subsequent intiacranial complications develop Meningitis is the complication usually encountered As there is an interval of from one to several weeks, as a rule, between the initial infection and the time when complications occur, attempts to induce a state of active acquired immunity should receive consideration The vaccination was begun as soon as the bacteriologic diagnosis was made. It was

necessary of course to culture material taken from every infected mastoid bone at operation so that this form of therapy could be employed

The vaccination technic originally consisted of six intradermal injections administered at the rate of two a week in the following increasing doses: 0.1, 02, 03, 05, 08 and 1 cc For doses larger than 02 cc several simultaneous miections were made During the past two years four additional subcutaneous injections have been added. The first inoculation was given within 48 hours after the operation or, occasionally, before the operation In the latter instances, the bacteriologic diagnosis was based on cultures of the discharge from the middle ear To avoid loss of time, a stock vaccine was used for the initial injection For the remaining injections an autogenous vaccine was employed

Sixty-one patients with acute mastoiditis due to infection with the type III pneumococcus were admitted to the hospital between September, 1931, and April, 1937 Of these, 56 received a full course of the vaccine In the remaining five cases, no vaccine or only one or two injections were given because of deaths occurring shortly after operations The five deaths were caused by facial erysipelas, accompanied by hemolytic streptoccus bacteremia in two instances, by meningitis which was present on admission to the hospital in two and by meningitis resulting from an operative injury in one

Of the 56 patients who had received a full course of vaccine, four died In one patient a woman 66 years old, bronchopneumonia developed six weeks after her operation and three weeks after her discharge from the hospital The remaining 52 patients who received full courses of vaccine made uneventful recoveries

Of 964 patients admitted to the Mount Sinai Hospital with acute mastoiditis during the ten years (from 1921 to 1931) prior to this work, 40 had mastoiditis due to infection with the type III pneumococcus Of these, 13 died of meningitis—a mortality rate of 32.5 per cent (The mortality rate for the previous years, from 1927 to 1931, was 22 per cent)

Action of Sulfanılamide in Meningitis—R Martin and A. Delaunay,33 after reviewing the literature, stress the slight toxicity of sulfanilamide, pointing out that the toxic dose is from 20 to 50 times greater than the curative dose The therapeutic efficacy of sulfanilamide impressed the authors especially in a case of purulent streptococcis meningitis. The patient, a boy aged eight, had an extremely severe meningitic reaction Treatment with antimeningococcus serum proved ineffective After the bacteriologic examination established the etiologic rôle of a hemolytic streptococcus, treatment with sulfanilamide was begun Morning, noon and night the boy was given tablets of 05 Gm each by mouth At first the daily dose of sulfanilamide was 15 Gm, but it was increased to 2 Gm. and then to 3 Gm Under the influence of this treatment, the extremely desperate case had a favorable outcome The authors cite others who obtained favorable results with sulfanilamide in the treatment of streptococcic meningitis Many reports of a similar character have appeared in the literature E D Anderson³⁴ reported complete and rapid recovery in a hemolytic streptococcic meningitis of otitic origin Two other recoveries were recorded by M H Weinberg, R R Mellon and L E. Shinn,35 who urge early use of the drug and H B Smith and E H Coon 36

F. F Schwentker and his collaborators³⁷ used sulfanilamide or its derivatives in the treatment of four cases of meningitis due to beta-hemolytic streptococci Two of the patients had a primary office focus and one a traumatic focus (craniotomy wound), and in the fourth no purulent focus was discovered In three patients surgical intervention (mastoidectomy, exploratory craniotomy) accompanied therapy with sulfanilamide or its derivatives. Three patients received intraspinal therapy with these chemicals while, in the other patient, oral therapy alone was used Three patients recovered and one died It appears that sulfanılamıde or its derivatives offer the possibility of a specific chemotherapeutic approach to the treatment of beta-hemolytic streptococcus meningitis A combination of oral and intraspinal therapy seems to deserve a thorough trial If the patient is not nauseated and can swallow, treatment should be started with sulfanilamide by mouth and also by the intraspinal route Tablets are used for oral administration. The total dose for the first 24 hours is calculated on the basis of three tablets (1 Gm) to each 20 pounds (9 kg) up to 100 pounds (45 kg) of body weight For adults with acute infections the authors believe that 5 Gm of this substance represents the maximal daily dose. This total amount is divided into four doses given at intervals of six hours. In preparing the drug for clinical use it is their practice to dissolve 0.8 Gm in 100 of physiologic solution of sodium chloride which has been brought to the boiling point and then cooled to about 194° F (90° C) Such 08 per cent solutions of sulfanilamide may be used intrathecally The general practice in administering the drug intrathecally should closely follow that recommended for the use of antimeningococcus serum in meningococcic meningitis, namely that rather complete spinal drainage by lum-

bar puncture should be instituted and then from 15 to 25 cc. of a warm, freshly prepared, 08 per cent solution of sulfanilamide should be permitted to flow in by gravity If the patient cannot swallow tablets, parenteral therapy by the subcutaneous route with either hydrochloride of 24 diaminoazo-benzene-4' sulfonamide or an 08 per cent solution of sulfanilamide in sterile physiologic solution of sodium chloride may be instituted. With the former solution, 1 cc per pound of body weight constitutes the total daily dose This is divided into four equal doses given at intervals of six hours If 08 per cent sulfanilamide solution is used, it should be given as a hypodermoclysis in the following amounts For patients up to 40 pounds (18 kg) 100 cc from 40 to 80 pounds (18 to 36 kg) 200 cc, from 80 to 120 pounds (36 to 54 kg) 300 cc and for those weighing more than 120 pounds 400 cc in 24 hours. Therapy should be be continued at the advised level until the spinal fluid has been rendered sterile for at least 48 hours and a marked general improvement in the patient's condition has occurred At this point the intraspinal therapy may be discontinued and the amount of the drug given by mouth reduced by one third Adequate oral therapy should be maintained until the patient is entirely well Surgical procedures designed to eradicate septic foci are indicated in streptococcic meningitis as an adjunct to specific therapy, but extensive surgical intervention should not be resorted to until the infection has been brought under control by specific therapy

Both sulfamilamide and prontosil exhibit marked therapeutic effects in mice against hemolytic streptococcus infections according to the observations of R R Mellon, P Gross and F B. Cooper.³⁸ This effect obtained for strains

of both medium and high virulence. Their experiments show no indication that phagocytosis is a factor in the mechanism of the therapeutic action of these drugs. Proper treatment of guinea-pigs with sulfanilamide results in a localization and rapid healing of experimental intradermal hemolytic streptococcus infections, which in the untreated animal may desseminate with fatal results. No qualitative changes in the character of the histologic response to the hemolytic streptococcus as a result of sulfanilamide administration were noted.

There have been numerous warnings against indiscriminate use of sulfanilamide Particularly serious are the possible dangers of granulocytopenia and sulfhemoglobinemia. The latter may sometimes go unrecognized without adequate methods of diagnosis. The complication originally called enterogenous cyanosis, thought to be due to "intestinal toxemia," has been shown to be due to the presence of sulfhemoglobin or methemoglobin in the blood

Sulfanilamide should not be administered in association with other drugs until definite information is available as to toxic effects. Thus far only the harmlessness of sodium bicarbonate in such association seems to have been established. Magnesium sulfate and some of the coal tar derivatives are conspicuously drugs which should not be administered concurrently.

Premature publicity for this drug has, as usual, been unfortunate. The startling news reports that the administration of sulfanilamide will "cure" gonorrhea in 48 hours has led to some unpleasant results. Responsibility lies with pharmacists who are willing to sell dangerous drugs to anybody over the counter. In one large city, hospitals have admitted patients with severe sulfhemoglobinemia resulting from self medication with sul-

fanilamide. The physician must bear in mind the potential hazards of this drug.

Brain Abscess

The treatment of abscess of the brain, at least after the acute stage, nearly always involves incision or at least aspiration of the collection of pus. It, therefore, becomes all the more evident. according to S L Shapiro³⁹ that the physician should be on the watch for possible errors in diagnosis to avoid unnecessary traumatization and possible infection of a sterile brain. A case is cited to illustrate a condition which from this standpoint is peculiarly like to serve as a pitfall for the otologist Coincident with or after operation, the patient showed choked disks, increased pressure of the cerebrospinal fluid, frontal headache, vomiting and some evidence of incoordination suggestive of cerebellar involvement on the right side All these symptoms disappeared in the course of four weeks, and the patient has remained perfectly well for over two years Increased intracranial pressure without actual involvement of the brain accompanying suppurative conditions in the ear has been described several times

The condition underlying manifestations of increased intracranial pressure without actual intradural involvement has been variously termed serous meningitis, spinal arachnoiditis of the posterior fossa, cystic arachnoiditis and precerebellar cyst All these names have a common substratum in that they assume the symptoms to be the result of an unusual accumulation of fluid in the cerebellopontile cistern, which may either communicate with the other subarachnoid spaces or be shut off by adhesions to form a cystlike collection of fluid between the dura of the posterior fossa and the cerebellum adjacent to the petrous bone In the first instance it may be

absorbed or cured by a lumbar puncture, in the second the fluid must be evacuated through an incision in the dura.

There are present no cases in which postmortem records or histologic studies of material removed at autopsy are available There are, however, a considerable number of case reports involving cystic arachnoiditis mistaken for acoustic or cerebellar tumor which serve to shed some light on the subject. The belief has been expressed that a previous otitis media is frequently the etiologic factor in producing this low grade inflammation of the arachnoid membrane It is probable that a similar process is responsible for the symptoms in those cases of suppuration of the ear in which there are signs of increased intracranial pressure without actual involvement of the brain

A S Fernando and G de Ocampo⁴⁰ report a case of otogenic cerebellar abscess with recovery The patient was admitted with symptoms definitely pointing to labyrinthine disturbance. The hearing and caloric tests showed that the labyrinth was completely irresponsive, but also there were phenomena which could not be explained by this condition alone The direction of the nystaginus, which was toward the diseased ear and which was not to be expected in a destroyed labyrinth, the continuous headache and insomnia and the mode of falling made the authors suspect some intracranial involvement besides the diffuse suppurative labyrinthitis This was strengthened by the presence of slight rigidity of the neck on the day before operation, which prompted the lumbar puncture that showed serous meningitis. The meningitis was more or less of the irritative or protective variety. The presence of cerebellar abscess was quite evident, and on the morning of the operation (Newman-Jansen endocranial technic) additional though vague localizing symptoms appeared in the form of weakness of the grip of the left hand and adiadokokinesia When labyrinthitis and cerebellar abscess occur together the symptoms are confusing The patient was kept in the hospital for almost four months Maximal drainage and minimal traumatism were assured by cautious insertion of a rubber drain. The pus obtained from the abscess was sterile, probably owing to the disintegration of the bacteria by some unfavorable tissue reaction The route of infection must have been through the labyrinth Lumbar puncture made three months after operation revealed normal spinal fluid showing that the patient had recovered completely from the otogenic serous meningitis

Treatment—The treatment of cerebral abscess was recently discussed by C Vincent of Paris 41 He described a new surgical treatment of intraparenchymatous abcess of the cerebral hemisphere His point of departure was the practical observation that, if life is imperiled by a brain abscess, the edema that forms in the neighborhood of the abscess is more largely responsible than the general infection. This edema may lead to an increased pressure on the brain and to the compression of vitally important Consequently, the next consideration after localization of the abscess focus is how this compression may be relieved Vincent has already carried out a procedure to relieve pressure in 12 cases The astonishing thing about the therapeutic course of these cases was that as soon as the compression was relieved the menacing general symptoms (cachexia, anorexia, vertigo and headache) completely disappeared and a distinct period of convalescence began So extensive was the subjective improvement that the patients felt themselves

cured. No indication of a cerebral process could be detected from a neurologicobjective standpoint in some of the cases, despite the fact that the abscess was still present

After commenting on Vincent's report, Albrecht cautioned against the dangers of encephalography and pointed out the significance of alterations in the cerebrospinal fluid, such as the increased number of calls, the increased protein content and the alterations in the curve in the colloidal gold test

Sauerbruch laid strong emphasis on the fact that an acute cerebral abscess may exhibit all the signs of a typical inflammation in other organs. Hence Vincent's procedure, while not to be depreciated, ought unqualifiedly to be confined to those chronic cases in which the suppurative foci tend to encapsulate

Sinus Thrombosis

A clinical analysis of thrombosis of the sigmoid sinus is presented by J H Maxwell 42 In contradistinction to a rather prevalent idea that the presence of sinus thrombosis is practically always an indication of a long-neglected acute suppurative mastoiditis, one must recognize that this condition may develop within the first week of otitis media by extension either to the sigmoid sinus or to the jugular bulb. In those cases of sepsis occurring during the first few days of the aural suppuration, thrombosis, if present in the sigmoid sinus, usually has developed by the thrombophlebitis route. One should not wait until organisms are found in the blood stream before one intervenes surgically

In every case of suppurative mastoiditis in a septic patient the sigmoid sinus should be **exposed widely** for examination during the operation even though the sigmoid plate is intact. The degree of sepsis present in sinus thrombosis

varies depending perhaps on the rate of entrance of bacteria into the blood stream and the bactericidal qualities of the patient's blood serum. The prognosis for recovery from sinus thrombosis may be said to be good in patients who receive early diagnosis and adequate treatment.

Treatment of thrombosis of the lateral sinus without ligation of the internal jugular vein is advocated by M S Ersner and D. Myers, 43 who feel that thrombosis is a protective process and that ligation is not a panacea Ligation of the internal jugular vein does not prevent metastasis, embolism or septi-Treatment of infection of the lateral sinus is primarily medical and partially surgical The surgical principle is the institution of drainage and the avoidance of over manipulation Thrombectomy is not indicated when the thrombus is firmly fixed The internal jugular vein should not be ligated when infection is present, but drainage should be instituted by means of incision Ligation is not the crux of the situation Recovery depends on the resistance of the host and its protective elements, according to our experience the thrombus is one of the mechanisms in the line of defense

The medical treatment is primarily concerned with the septic symptoms that the patient manifests The transfusion of whole blood is probably one of the most important single modes of therapy In addition to transfusions of whole blood, whenever practicable or available immunotransfusions, specific or nonspecific are recommended. The use of specific serum when available should be instituted During the past year the use of sulfanılamıde (para-amıno-benzenesulfonamide) has attracted considerable attention The literature is full of glowing reports concerning its use. The use of quinine dihydrochloride in the presence of chills, given in frequent doses until the patient complains of tinnitus aurium, occasionally yields beneficial results

The first step in the surgical attack is to eradicate the focus or the source of the infection (a) If symptoms suggesting sepsis are present in cases of otitic infections, immediate *mastoidectomy* should be performed and the lateral sinus exposed for further study and observation In the meantime, expectant treatment is instituted (b) If septic symptoms indicative of involvement of the lateral sinus occur after mastoidectomy, the mastoid should be revised and the sinus exposed for inspection

- C McDougall⁴⁴ reviewed the otologic literature of the past ten years and was impressed with the fact that of the 30 cases of lateral sinus thrombosis with joint and muscle metastases which had been reported, there were only three mortalities On the subjects of diagnosis and treatment the author concludes
- 1 Blood cultures are of a great aid in diagnosing lateral sinus thrombosis Over 50 per cent of the diagnosed cases show negative growth after repeated cultures. We must not put too great dependence on the result of a negative blood culture in making a diagnosis of this infection
- 2 Whole blood transfusions, with properly typed donors, should be given to all septicenias with a low red blood cell count and low percentage of hemoglobin
- 3 Intravenous injections of *mercuro-chrome*, 220 soluble, are a valuable therapeutic aid in septic thrombophlebitis when given intelligently, early, often and not in too large a dose at one time
- 4 It is my observation from these cases and several others recently reported, that joint and muscle metastases

- occur mostly in children and where they exist as a complication of septic thrombophlebitis of the lateral sinus, the prognosis is favorable under proper treatment. These lesions also more frequently follow sinus thrombosis from acute infections of the middle ear rather than chronic otitis.
- J M. Nielsen and C B Cowiville⁴⁵ discuss intracranial complications of otogenous thrombosis of the lateral sinus and conclude
- 1 The intracranial complications of otogenous thrombosis of the lateral sinus are usually due to venous obstruction or to retrograde extension of infection into the afferent vessels and from thence into the meninges or brain. The anatomic arrangement of the intracranial venous system accounts largely for the distribution and character of many of these lesions.
- 2 The intracranial lesions which may follow thrombosis of the lateral sinus may be benign and transitory (local edema of meninges and brain, serous or reactive meningitis) or malignant and often lethal (subdural abscess or hemorrhage, septic meningitis) extension into the venous channels with red softening (nonsuppurative encephalitis) or abscess formation
- 3 All focal lesions (edema, red softening, subdural or encephalic abscess) may be found in almost any situation in the intracranial space due to the communications in various parts of the venous system
- 4 In most of the fatal cases of otogenous thrombosis of the lateral sinus some other intracranial lesion is found at autopsy These lesions may be coincidental, developing as a result of extension along some other path from the middle ear, or consequential, due directly to the thrombus in the lateral sinus

- 5 Transitory cerebral or cerebellar symptoms result from stasis in the local veins (local edema of cortex or meningitis) or to non-infected thrombosis (red softening) or infected thrombosis (septic meningitis, subdural or encephalic abscess) of these veins
- 6 Transitory symptoms may follow abrupt (operative) occlusion of the lateral sinus or jugular vein if there is no pre-existing thrombus in the sinus.
- 7 The character and location of localized meningeal and cerebral lesions is determined by a study of the neurologic symptoms and signs and a survey of the clinical course of the lesion
- I N Novick46 reviews the subject at length with special reference to (1) Anatomy of the lateral sinus and its tributaries, (2) physiology of the blood circulation through the brain, (3) etiology and mechanism of thrombosis, (4) types of thrombi and sequellae Novick maintains that in a given case of lateral sinus thrombosis, established definitely, one should not act hastily With very few exceptions, this is not an emergency in which one has to rush in and ligate the jugular vein immediately. The patient should be carefully observed and treated medically as long as his condition permits, and just as soon as the surgeon feels that more radical measures are essential he should reopen the mastoid wound or do a mastoidectomy if this has not been done, then the sinus should be packed above and below, incised and tested for bleeding from each end If there is bleeding from both ends and the blood is coming from the sinus itself and not from its tributaries, it may be assumed that there is no thrombosis in any part of the sinus or the jugular vein the sinus should be packed and the mastoid incision dressed. If, however, there is bleeding from below and none from above, there is a thrombus somewhere

between the upper plug and the torcular herophili. The thrombus should be looked for and removed, if possible, the sinus packed and the mastoid wound dressed Ligation of the internal jugular vein in this instance will be of no further help, since in this area there are many other pathways by which it is possible for the infection to gain entrance to the systemic circulation. On the other hand, if bleeding is obtained from above, which means that a thrombus is in all probability present either in the bulb or in the vein itself, ligation of the internal jugular vein, followed by the removal of the clot, is justified and should be done

SKULL FRACTURE

Fracture of the skull involving the paranasal sinuses and mastoids is discussed by C C Coleman 47 Such fractures are of importance mainly because they expose the brain to infection Less serious effects are paralysis of cranial nerves and facial deformity from displacement or loss of bone fragments The main purpose of Coleman's discussion is to emphasize the dangers arising from infection in fracture of the base of the skull The first eight cianial nerves are hable to injury from fractures which traverse the paranasal sinuses or mastoid Blindness of one eye, extra-ocular palsy and anosmia are not with fractures of the anterior fossa Unilateral blindness and deafness are usually permanent Oculomotor involvement with dilatation of the pupil, due to fracture, comes on immediately while later dilatation of one pupil indicates a homolateral clot Facial paralysis following fracture of the skull is rarely permanent It usually appears a few days after injury Inflammation is probably the chief cause of this paralysis Permanent paralysis of the nerve requires anastomosis with another healthy motor cranial nerve

Fractures of the skull, whether of the vault or base or, as they usually are, of the two in combination, frequently produce serious damage to the brain, and the brain injury should receive primary consideration Fracture of a paranasal sinus is often only a minor effect of an injury which damages important regions of the brain at the base of the skull and severely macerates the cerebral cortex by the indriven fragments of an associated compound fracture of the vault Consideration of the sinus fracture in serious cases of head trauma must at times be postponed or even entirely abandoned in favor of a management which gives the patient the best chance to withstand the primary effects of his injury The two main objectives of surgical treatment of head trauma are the prevention of infection and the removal of intracranial hematomas

The limitations of the x-ray examination in the demonstration of fracture lines at the base of the skull are well known, and the diagnosis must generally depend on such effects of the fracture as bleeding from the cianial orifices, cerebrospinal fluid leaks, suggestive ecclymoses and palsy of the cranial nerves

Compound, depressed fractures of the frontal region frequently involve the frontal sinus, with extension of the fracture line into the floor of the anterior fossa and through the ethinoids. Patients with fractures of this type, notwithstanding the severe laceration of the frontal lobe, are often free from shock, and early operation for the prevention of infection should be done.

Depressed fracture of the outer wall of the sinus is not infrequent. This fracture, while often compound both externally and internally, is sometimes unique in being confined to the sinus and often

requires no treatment other than disinfection, excision and suture of the cutaneous laceration. The frontal sinus may be involved in linear fractures which radiate from the vault, and in these cases there is much difference of opinion as to treatment.

Sixty-one cases of dizziness from a series of 325 cases of head injury in order to determine the cause of dizziness in head injuries and the value of vestibular tests as a diagnostic adjunct, as well as the ability of the patients to prognosticate the duration of dizziness were analyzed by M A Glaser 48 The vestibular tests are of no value in determining either the type of dizziness or the presence or absence of dizziness encountered in these patients, nor by them can the duration of dizziness be prognosti-They do, however, in certain cases, reveal the presence of pathologic change within the brain and thus corroborate, to a degree, the truth of the patient's story with regard to a head injury. In this manner, they are indirectly of value in eliminating the malinger It is quite evident that the common types of dizziness associated with head injuries are not dependent on definite vestibulai lesions, instead, it is likely that they are due to an entirely different mechanism, possibly transient cerebral vasomotor disturbances Encephalograms and vestibular tests, performed on four patients, both demonstrated pathologic changes in the central part of the brain In two of these patients dizziness was entirely absent Vestibular tests performed in 66 cases revealed subjective symptoms in 80 per cent, objective neurologic signs in 21 per cent and vestibular abnormalities in 76 per cent Objective signs were thus demonstrated more frequently by vestibular examination than by clinical neurology Though no distinct vestibular complex was asso-

ciated with head injuries, there were certain predominant observations. Normal vestibular responses may indicate either an undamaged brain or a brain evidencing pathologic change which has not involved the vestibular pathways. Lesions of the end organ signify peripheral involvement of the vestibular fibers, while central lesions indicate pathologic changes either directly present or adjacent to the central vestibular pathways.

J T Travers⁴⁹ has found encephalography of definite value in the study of posttraumatic sequels, and particularly in the differential diagnosis of subdural hematoma Encephalographic studies revealed a marked shift of the ventricular system to the side opposite the lesion, with compression and deformity of the ventricle on the side of the lesion, or (in one instance) a failure to demonstrate this ventricle at all Failure of the subarachnoid space to fill on the side of the lesion was also discerned in another instance

Fehr and Meier⁵⁰ present an analysis of the results of conservative treatment of the fractures of the base of the skull In 17 years (from 1919 to 1935), 417 patients with fracture of the base of the skull were admitted to the university clinic of Zurich The conservative treatment consisted of rest in bed for from three to four weeks, application of an icebag and administration of methenamine The lumbar puncture for diagnostic purposes as well as to influence the rising intracranial pressure was widely employed With the exception of a single case of meningitis, which developed following the lumbar puncture and was associated with a sudden closure of the aqueduct of Sylvius, there were no untoward symptoms observed as the result of the procedure The authors likewise observed good results

from intravenous administration of hypertonic solution of dextrose. As a rule, from 40 to 100 cc. of a 20 to 40 per cent solution, frequently with the addition of methenamine, was administered daily. The total mortality amounted to 324 per cent Among 383 cases in which conservative treatment was resorted to there was a mortality rate of 28.3 per cent Thirty-two patients were submitted to operative intervention, with a mortality rate of 81 per cent. The treatment of basal fractures, in the opinion of the authors is the domain of the surgeon in co-operation, however, with the neurologist and the eye and ear special-

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DISEASES OF THE PHARYNX

By A R HOLLENDER, M D

TONSILS AND ADENOIDS

Focal Infection

The nose and throat in relation to theumatic diseases is discussed by H Barwell,1 who asserts that an attack of acute rheumatism or rheumatic fever is normally preceded by an acute infection of the fauces with a hemolytic streptococcus, which often is only of slight severity It is usually a clinically mild and transient infection of the throat that precedes the most severe attacks of rheumatic fever After this there is a symptom-free interval of from a few days to a few weeks before the onset of rheumatic symptoms Further attacks or recurrences, or acute rheumatism are similarly preceded by streptococcic pharyngitis. There is little room for doubt, then, that acute theumatism is caused by streptococcic infection, but the mechanism by which the effect is produced is still uncertain. It does not appear to be a septicemia, and suppuration never occurs, it seems rather to be related to a faulty method of dealing with bacterial toxins There seems to be a definite delay in the immune responses of rheumatic, compared with those of nonrheumatic people, and the patient who develops an attack of rheumatic fever "handles the products of the hemolytic streptococcus ın a peculiar way" (Coburn) It would seem to be this peculiar response which determines the incidence of acute rheumatism The incidence of acute infection of the fauces is diminished by tonsillectomy. When, therefore, a sore throat has been followed by rheumatic fever, it is proper that the tonsils should be removed. But numerous smaller nodules of lymphoid tissue remain scattered over the pharynx, and acute pharyngitis can and does occur after tonsillectomy, so that this operation does not with certainty prevent recurrence of acute rheumatism, though it makes it less probable

Five cases, representative of a series of 23, are presented by T P O'Connor,² which display the typical symptoms of labyrinthine irritation in the absence of any suppurative process in the brain, middle ear, inner ear or mastoid Common to each was a subacute or chronic nasopharyngitis that harbored Streptococcus viridans Treatment and eradication of this focus was followed by prompt subsidence of all symptoms

The manner in which the infection of the nasopharyngeal mucous membrane produces labyrinthine symptoms is a fruitful field for conjecture. The most likely explanation appears to be an absorption into the blood stream of the toxins elaborated from the infection and a secondary irritation or stimulation of the labyrinthine structures. The proximity of the involved area to the Eustachian tube and the middle ear appears to be merely coincidental. Further investigation of this point and into the possibility of any specificity of the offending organisms is contemplated.

Tonsil and Adenoid Operation

The results of 76,000 adenoid and tonsil operations are reported by W H Turnley ³ This large series of cases operated upon for the removal of tonsils or adenoids, or both, included patients from six months to 72 years of age, and of every race and color But six of this

number died, none of them from hemorrhage None of the others suffered any disturbed function following the operation Minor discomforts occasionally were complained of, consisting of dry throat and bad taste in the mouth, a slight speech defect lasting a short time, due to paralysis of the soft palate, and bronchial colds instead of their former head colds

There are few contraindications to tonsillectomy, as persons over the age of 50 are given a thorough physical examination and children under the age of two are not operated upon unless there is a history of repeated colds and sore throat with enlarged glands of the neck, otitis media, etc. In these patients the adenoids are removed and occasionally the tonsils also In this series 3172 patients were operated upon because they complained of "iheumatism" -- painful joints, bones, nerves, muscles and fascia After six years, 83 per cent of this number are improved or cured, 12 per cent show no improvement and five per cent Of those who showed no are worse improvement or became worse, some other foci of infection was present, also they were past their youth or had some bony changes take place The younger the patient and the shorter the duration of the rheumatism, the better the results, and vice versa

Patients with heart lesions are probably not as much benefited as those with rheumatism. In a series of 1000 patients with valvular lesions no deaths occurred. This does not substantiate the general opinion that these patients do not tolerate ether well. No decompensated heart cases are operated upon

"The removal of tonsils lessens the incidence of sore throat about 90 per cent, for the reason that a sore throat is fundamentally tonsillitis. No cases are operated upon within ten days following

an acute attack Keratosis leptothrix is usually cleared up by the removal of tonsils, likewise a stubborn Vincent's ulcer of the tonsil Nonspecific chronic laryngitis is greatly helped Naturally, a quinsy cannot develop after a tonsillectomy unless there is a piece of tonsil tissue left, but an occasional retropharyngeal abscess may occur"

Adenoidectomy, thoroughly performed will reduce the incidence of otitis media in children 95 per cent Removal of adenoids in adults will greatly relieve tubal catarrh, otalgia is less often relieved

Some cases of iritis are benefited by tonsillectomy

That the lymphoid tissue in the nasopharynx occasionally involves the eustachian tube, both by blocking effect and by its being the source of infection for the middle ear is well recognized. This, in the opinion of D Roy4 accounts for the lessened frequency of involvement in the middle ear since there has been such universal removal of tonsils and adenoid tissue The paper deals with cases in which operation has previously been performed and remnants of this lymphoid tissue either still remain around the nasopharyngeal opening of the eustachian tube or have undergone compensatory increase in size

The author with the nasopharyngo-scope has found lymphoid tissue apparently in the mouth of the tube itself—and this usually several years after removal of tonsils and adenoids In the rapid routine of office practice the physician too often fails to make a thorough examination of this part of the nasopharynx and for this reason one is sometimes surprised at not obtaining the desired results from inflation with the catheter. Many examiners have seen particles of lymphoid tissue left after operation, which in a few years result in the return of the adenoids, and one

is faced with the necessity of advising a second operation While the effect of this lymphoid tissue on the eustachian tube must be considered, the problem of the method of treatment which is most applicable to the condition has frequently presented itself The author rejects the use of surgical instruments because they usually cause irreparable damage or are otherwise inadequate The use of the galvanocautery and surgical diathermy has been advocated by certain workers, but in his hands, Roy has found chemical cauterization most satisfactory for the destruction of lymphoid tissue located around and inside the tubal orifice

F W Merica⁵ as a result of his study advocates tonsillectomy as a cure for peritonsillar abscess. In 21 cases, the patients ranged in age from 13 to 56 years. There were no complications in any case, and each patient showed immediate improvement.

Anesthesia—As a rule, general anesthesia is preferable. It enables the operator to obtain a better exposure than is possible with the area under a local anesthetic, because the patients have difficulty in opening their mouths. With the aid of the suction machine and with the patient in the recumbent position, there is less likelihood of aspiration of pus. In a series of 21 cases, local anesthesia was used once, n-methylcyclohexenylmethylmalonylurea once, tribromethanol in amylene hydrate once and nitrous oxide induction followed by ether in the remaining eighteen cases.

Technic—An incision is made just through the mucosa, following the anterior pillar and down the posterior pillar. Then, with slight traction on the tonsil in the upper portion, dissection is started in an endeavor to free a portion of the upper pole before the abscess is ruptured. Then, with a suction tip following the knife, the incision is made

into the abscess cavity and the abscess is drained completely with the suction tip This relieves tension immediately, and with the upper pole practically free, the tonsil is easily lifted from its bed. with a small amount of dissection, it is loosened from the anterior and posterior pillars, a snare is slipped over the mass and the tonsil is removed with little difficulty Occasional bleeding from the pillars or in parts of the fossa After this procedure is completed and all bleeding is stopped, the other tonsil is removed This makes it unnecessary for the patient to undergo any further surgical treatment at a later date Complete healing is obtained in approximately the same length of time as after tonsillectomy done under ordinary circumstances

According to A H Neffson and J Brem⁶ faucial diphtheria, particularly in adults, may simulate peritonsillar abscess. The high mortality rate and prolonged convalescence of the survivors are directly attributable to unnecessary surgical manipulation and delay in the administration of antitoxin.

Whenever a patient with a supposed peritonsillar abscess is examined, diphtheria should be ruled out by repeated cultures. Incision of the peritonsillar tissues should not be done hastily. By following this conservative routine, it is hoped that the high mortality and the prolonged morbidity in this condition will be reduced.

Abscess

Complications — Complications secondary to peritonsillar and lateral pharyngeal abscess go frequently unrecognized until autopsy is performed. A review is given by C. T. Porter⁷ in which there are several interesting and pointed case reports

Method of Infection — It is contended that the pharyngomaxillary fossa

is most important. Porter is convinced that a great many of the secondary complications, such as septic emboli, are liberated through the petrosal veins and the torcular to the general circulation from an infected sinus above the jugular bulb

Retropharyngeal Abscess - Early diagnosis of retropharyngeal abscess is important, according to H Dintenfass 8 It is always a dangerous condition, and neglected cases frequently lead to death Cases have been reported in which death ensued as a result of hemorrhage from erosion of the internal carotid artery and still others in which the jugular vein had become thrombosed with consequent bleeding or sepsis The bacteriology of retropharyngeal abscess gives evidence that the predominating exciting microorganism is the hemolytic streptococcus, less frequently the staphylococcus and pneumococcus A number of conditions should be differentiated from retropharyngeal abscess, chief of which are enlarged thymus, meningitis, laryngeal diphtheria, severe adenitis, foreign body in the larynx, osteomyelitis and tuberculosis of the cervical spine

The treatment of retropharyngeal abscess in the beginning consists of the application to the neck of hot moist compresses, which are changed frequently In addition steam inhalations and hot gargles whenever possible and the injection of nonspecific protein may prove of value When the stage of suppuration is reached, the one curative treatment is operation Suction is employed to complete the evacuation of the abscess Improvement following the initial discharge of pus may be only temporary, and renewal of symptoms may occur as the result of the closing together of the wound edges This necessitates a further introduction of closed forceps followed by more suction The procedure may have to be repeated for several days until a cure results. If the retropharyngeal abscess has broken through into the parapharyngeal space and an incision in the pharynx is inadequate to drain the abscess cavity properly, an external incision is necessary. External incision should always be made if the abscess is tuberculous in character and has its origin in the vertebrae. In cases of hemorrhage from a ruptured carotid artery or jugular vein, or septic phlebitis of the jugular vein, ligation of the particular vessel is indicated.

Infections in Neck

Neck infections are discussed by G E Black who summarizes his study (1) The most common swellings of the neck are those due to infected lymph nodes (2) Infection in the neck may be either deep or superficial in origin (3) The course of deep infections of the neck depends very much upon the fascial planes (4) The treatment depends upon the etiology and the surgical anatomy of the part involved Points demanding emphasis are The blood picture may remain negative when a phlebitis is present, even though the blood has been drawn from the vem involved very shortly after the onset of the chills, torticollis from infection under the sterno mastord muscle is to the opposite side, and from infection along the paravertebral and trapezius muscles is towards the same side, the degree of the external swelling is no indication for the decision in necessity for external drainage

Cervical gland abscesses usually remain superficial and localized, but we keep in mind that the infection can and frequently does spread to the deeper structures. The sepsis may go on to fatal termination without an apparent increase in severity of the local symptoms. The ears should be inspected frequently, there

may be a tympanomastoid complication Adequate drainage can usually be obtained through the external route, and if internal drainage has been established and does not bring about almost immediate cessation of the infection, external drainage should be established without delay. In most all surgical procedures of the neck, the use of the knife is limited. Blunt dissection should be resorted to at the very earliest part of the operation possible.

Mediastinitis

More recent investigations of mediastinitis have revealed a number of interesting facts A C Furstenberg and Luis Yglesias 10 present important aspects with reference to the anatomy of the neck and mediastinum. Thoracic surgeons are more or less unanimous in the opinion that suppuration below the fourth dorsal vertebra calls for posterior drainage Such processes, which occur low in the mediastinum, may arise from disease of the esophagus, causes of the thoracic vertebrae or extension from the abdominal cavity. These may be approached preferably and adequately drained by dorsal mediastinotomy, in which the thoracie civity if opened posteriorly by resection of ribs or by removal of one or more transverse processes with a portion of the attached 11b

Cervical mediastinotomy is a far more conservative measure and one which often serves admirably to drain infections in the upper portion of the mediastinum. When pus enters the mediastinum from the neck, this procedure would seem the one of choice. To drain an abscess through the tissues which it has invaded is, according to the authors, a surgical axiom which in no other region of the body can be more advantageously applied.

Cervical mediastinotomy, moreover, has been successfully employed in traumatic perforation of the upper part of the esophagus. Through this technic, foreign bodies which have perforated the walls of the esophagus have been recovered. Esophageal perforations are sealed with packing to avoid fatal mediastinal emphysema, and drainage of subsequent mediastinal infection is adequately established. This is a heroic measure, but one which definitely possesses life-saving possibilities for the unfortunate victims of this grave accident.

In cervical mediastinotomy, the right side of the mediastinum is, for anatomic reasons, the logical approach The three large arteries-innominate left common carotid and left subclavian-esophagus, trachea and descending aorta divide the posterior part of the mediastinum into a right and left compartment. The right compartment is the larger, it contains many more lymphatic glands and is therefore the site of predilection for inflammatory processes in this region A right-sided exposure of the posterior mediastinum is obviously the procedure of choice when there is reason to believe that infection has extended through the neck by the lymphatic route Of considerable importance also is the fact that the eosphagus on the left lies in close relation to the pleura as it enters the thoracic cavity, while on the right the pleura and the esophagus come in contact at a lower level behind the pericardium Thus, in approaching the mediastinum on the right, there is less risk of mury to the pleura

With the area under local anesthesia, an incision from 2 to $2\frac{1}{2}$ inches (5 to 6 cm) long is made over the anterior margin of the sternocleidomastoid muscle down to the suprasternal notch. When the sternocleidomastoid, sternohyoid and sternothyroid muscles have been exposed,

these structures, together with the contents of the carotid sheath, are retracted laterally, exposing the trachea and, at a deeper level, the right side of the esophagus It may be necessary to elevate the right lobe of the thyroid, in which event care must be taken not to injure the inferior thyroid artery, which enters the gland on its posterior surface close to its inferior pole. At this point one must choose to enter by blunt dissection either the anterior mediastinum, which lies between the trachea behind and the arch of the aorta in front, or the posterior mediastinum along the lateral wall of the esophagus A guide to the procedure of choice might be found in a study of the etiologic factors producing the abscess. If suppuration has descended into the visceral space, it is presumptive evidence that the inflammatory process within the mediastinum will be found in its anterior part, if, on the other hand, the course of invasion is along the retrovisceral space, the posterior mediastinum becomes the logical site of predilection A drainage tube is introduced, and suction is applied at frequent intervals Some advantage may be derived from postural drainage by placing the patient in the Trendelenburg position

MEMBRANOUS PHARYNGITIS

The fact that Vincent's stomatitis may appear as the end result of many debilitating diseases is becoming more and more manifest. G. W. Farrell and W. A. McNichols¹¹ conducted an interesting study on the effects of different therapeutic methods and came to the following conclusions.

1 The severity of the case is determined by the resistance of the individual and the virulence of the infecting organisms. This is aptly illustrated in the different types of patients we handle,

the lower grades and younger defective children always being more susceptible

- 2 In all cases and under all types of treatment, in order to get a proper lasting cure, we feel that thorough prophylaxis and scaling of the teeth, accompanied by the removal of all mechanical irritations, is as necessary a requisite in the treatment of this disease as the medicinal side of the treatment
- 3 Abstinence from cigaret smoking and alcohol is to be recommended during the infection
- 4 The slightest surgical procedure, even in the presence of the mildest types of Vincent's infection, is to be avoided
- 5 In most cases the disease becomes more acute the longer it is allowed to progress without treatment
- 6 Solution of hydrogen peroxide, USP, is the prime factor in curing \ incent's infection However, some of the cases may be assisted by the use of other medicaments, but one cannot be sure of a cure in all cases unless solution of hydrogen peroxide is used in conjunction with the other medicaments We also feel that it cannot be used to excess. In referring to the use of solution of hydrogen peroxide in this paper it was always used at least four times a day, full strength. The recoveries were quickened in some cases when it was used more frequently, that is, every two hours, instead of four times daily

Bismuth therapy of nonspecific acute angina is evaluated by A Monteiro, V Brasil, Jr and G Samfraio 12 As a result of their studies they reach the conclusion that whereas angina usually lasts a week bismuth therapy reduces it to from 24 to 48 hours. Since one, or at the most two, injections of bismuth cannot be harmful, the authors suggest that such an injection be given even if the diagnosis of acute angina is not quite certain. At the same time a specimen is

taken for bacteriologic examination. After 24 hours either the improvement of the patient or the result of the bacteriologic examination will indicate whether the condition in question is angina or diphtheria.

BLOOD DISTURBANCES

Infectious mononucleosis is described by H J Isaacs¹³ as a disease characterized by fever, enlarged and swollen cervical lymph glands, peculiar posture of the head, abdominal pain and an increase in the number of mononuclear cells of the blood The blood shows an absolute and relative increase in the nongranular mononuclear cells The white blood count varies between 15,000 and 30,000 Of the total number of cells, 80 to 90 per cent are of the nongranular type, and, according to Longcope, are in the following forms (1) Small mononuclear leukocyte, identical with the small lymphocytes, (2) large mononuclear cells identical with the large mononuclears, and (3) atypical mononuclear cells The differential diagnosis includes a large number of conditions It is the early usage of the heterophilic agglutination test that absolutely and specifically establishes the diagnosis of infectious Several case reports of mononucleosis other authors are reviewed and explanations offered as to the significance of the heterophilic reaction Concluding the author states (1) The heterophilic agglutination test is a specific test for infectious mononucleosis (2) Serum sickness also gives a positive response, but can be differentiated from above by the absorption test (Davidsohn)

The treatment of agranulocytosis on the basis of investigations carried on at the Frankfort University Medical Clinic, is presented by H. E. Bock ¹⁴. The discovery of aminopyrine agranulocytosis, the importance of which according to the

German point of view is greatly exaggerated, not only contributed substantially to the explanation of the pathogenesis but constituted an important landmark in therapeutics, since it demonstrated that, like barbituric acid preparations, aminopyrine preparations are to be avoided in disturbances resembling agranulocytosis Aside from this discontinuation treatment and the enormous importance of nursing care there is also an active therapy Whereas protein substance, epinephrine, thyroxine and liver substance (the last named important because of its general effect) represent only subthreshold granulotactic stimuli, induced turpentine abscess has a more durable effect

The three principal therapeutic procedures in agranulocytosis are roentgen stimulation-irradiation of the medullated bones. blood transfusions and administration of pentnucleotide. Although nucleotide in large doses has heretofore represented the most effective medication for the building up of leukocytes, a blood transfusion exerts the optimal general effect Copious and frequent transfusions should be performed and the utmost caution exercised in the Cases have been selection of donois reported in which three transfusions of 675 cc each were given and in other cases the quantity even reached 1000 cc Satisfactory biidging per transfusion over the most dangerous four initial days, that is, an effective compensation for granulocyte deficiency in the face of the threatening sepsis, is however not always achieved even by maximal transfusions if normal blood is used

Schittenhelm attained favorable results in a single case by utilization of the blood of a patient with myeloid leukemia Bock's employment of a similar procedure, undertaken without knowledge of Schittenhelm's case, was also successful. At the Volhard clinic a woman typist, aged 40, who presented a severe agranulocytosis, was placed out of danger within 19 days by twelve 500 cc. transfusions of leukemic blood patient on admission exhibited all signs of the disease in its most exaggerated form; for five days no granulocytes could be observed, the total number of leukocytes fluctuated between 200 and 1000 and there was no monocytosis The patient was highly feverish, the erythrocyte sedimentation rate was elevated, and marrow of the tubular bones exhibited a purely myeloblasticreticular high grade cell-deficient character Further complications were pneumonia The total and necrosis of the gums value of leukocytes transplanted corresponded to that contained in 250 transfusions of normal blood The transfusions were unaccompanied by any incident

The colossal consumption of leukocytes was especially exacerbated by a femoral abscess, which was opened at the end of the third week. Only in the fourth week did the leukocyte balance become positive. The high grade destruction of the myeloid tissue and the regeneration of myelopoiesis toward normal under the influence of the leukemic blood could be observed at all stages of the illness both in the hematomyelogram and in the histologic section of the sternal punctate.

PHARYNX

Tumors

H R Schinz and A Zuppinger¹⁵ review the results obtained at the Roent-genologic Institute of the University of Zurich in the treatment of malignant tumors of the epipharynx, mesopharynx, hypopharynx and larynx For tumors in this localization the authors consider protracted fractional distance irradiation

the method of choice Surgical treatment alone is no longer permissible with the exception of the case of laryngeal fissure in small cancers of the vocal cords The close range treatment, in the form of radium implantation of the intraoral radium pack, is to be considered only in tumors of the soft palate uncomplicated by metastases Electrocoagulation in later combination with radium implantation is utilized as an aid in the treatment of small residual tumors or recurrences of small size Regional lymph nodes are treated by irradiation mary surgical removal is not practiced The principal advantage of the distance irradiation carried out in the form of prolonged fractional treatment is the complete absence of deforming effect Of the 115 cases treated, 51 were tumors of the movable portion of the tongue, 31 of the floor of the mouth, 11 of the buccal mucosa, 13 of the alveolar process and gum, five of the hard palate and four extensive ones of the oral cavity whose origin could no longer be determined Hornified flat cell carcinomas medominated Other types were occasionally seen in tumois involving the hard palate. The authors consider radium implantation in the primary tumor and later removal of the lymph nodes, followed by irradiation, the method of choice in carcinoma of the movable portion of the tongue Protracted fractional distance irradiation alone, with a later radium implantation in the remnant of the tumor, was employed in the advanced stages of the disease For small tumors of the floor of the mouth the authors recommend, besides radium implantation, the use of a radium pack and protracted fractional distance irradiation for the advanced stage The same treatment is applicable to the carcinomas of the buccal mucosa The treatment of the tumors of the hard palate depends to

a great extent on the histologic character of the growth More or less roentgen resistant tumors, such as gland carcinomas, should be operated on tracted fractional distance irradiation is the only method to be considered in the treatment of diffuse tumors of the oral cavity More than half of their cases presented an advanced stage of the disease with extensive growth and frequently with regional metastases Thirtynine cases of oral neoplasm were treated between 1919 and 1928, but in only 20 was the treatment completed of the patients were alive one year later, five after three years and five after five years Of the last five patients only one was treated exclusively by surgery During the period 1929 to 1935, 76 patients were treated In 61 the treatment was completed ()f 40, 13 survived for a period of three years, and of 16, two survived a period of five years. The relative three- and five-year symptomfree period for the group treated between 1919 and 1928 amounted to 25 per The completely free three-year period for the group treated between 1929 and 1933 amounted to 32 per cent, and the relatively free to 40 per cent The results obtained with primary iiradiation followed by later surgical interventions were better than those obtained by primary operation and later irradiation. Two patients out of 32 were symptom-free after a three-year period under the latter treatment, while with the former 16 out of 49 were symptom-free at the end of three years The protracted fractional distance irradiation is capable of giving permanent results with extensive tumors of the oral cavity Of 22 cases of carcinoma of the buccal mucosa, seven were symptom-free for from one to four years

The difficulties of histologic diagnosis of malignant processes of the epipharynx

are pointed out by K Wolff ¹⁶ This writer calls attention to the great service rendered by Graff who showed (1) that the primary focus of a malignant growth may be situated in an obscure place such as the nasopharynx and its accessory cavities, and (2) that it is possible with proper technic to expose this area for purposes of examination

A description is given of two malignant processes of the epipharynx, in which the new technic of Graff was employed The cases are especially noteworthy because of the peculiar manner in which the processes spread and particularly because they show the histologic-diagnostic difficulties that are encountered in the examination of a single section first case, the post-mortem examination confirmed the existence of a tumor of the epipharynx The lymph nodes of the neck had nearly all become transformed into tumor-like nodules The lymph nodes of the pulmonary hilus were likewise enlarged However, the case history contains nothing regarding hyperplasia of the lymphatic tissues of the intestine The most surprising aspect was presented by the stomach, for tumor nodules were found in all portions of its mucous membrane The tumor in the epipharynx gave at once the impression of a maligrant growth

After giving a detailed description of the histologic aspects, Wolff states that on account of the various cell forms it might be justifiable to think of "the peculiar tumors suggesting gianulomas," which Kiauspe had observed in the upper air passages and in the digestive tract Krauspe suggested the term sarcomatous reticuloendotheliosis. Wolff says that in the reported case a sarcoma existed, which originated in the reticulum. After demonstrating that the process was neither lymphogranulomatosis nor lymphosarcoma, he concludes that the growth

was a retrotheliosarcoma In the second case the aspects of chronic inflammation predominated However, a cervical lymph node revealed signs of malignant growth Finally, it is emphasized that in case of a tumor in the region of the neck, in which the origin is obscure, the region of the nasopharynx should always be carefully examined

Glossopharyngeal Neuralgia

Glossopharyngeal neuralgia associated with abscess of the petrous tip following mastoiditis is discussed by H P. Schugt 17 A case is described in which the pain cleared up almost immediately on dramage of an abscess of the petrous tip Instances of simultaneous disturbance of the glossopharyngeal, vagus and spinal accessory nerves are known as Vernet's syndrome The syndrome may result from fracture of the skull, tumor of the brain, syphilitic meningitis, abscess or tumor of the petrous tip, thrombosis of the bulb of the jugular vein or any inflammatory process in the region of the jugular foramen Involvement of obscure etiology in the soft palate, the vocal cords or the sternomastoid or the trapezius muscle may originate in trauma or disease of the area adjacent to the jugular foramen or in a pathologic condition of the petious tip

Glossopharyngeal neuralgia is considered by W B Hoover and J L Poppen, 18 who review the literature, suggest points for differential diagnosis and then describe the treatment. This may be either medical or surgical Trichloroethylene is the only drug which has given a marked amount of relief for this condition. It is administered by the patient's inhaling from 15 to 30 drops from three to four times a day. The patient is instructed to lie down, drop the required number of drops into a gauze pad or kerchief, place it over the

nose and inhale the vapor as long as he can smell the trichloroethylene This inhalation is to be repeated three or four times a day.

The surgical treatment of choice is the intracranial section of the ninth nerve in the posterior fossa. The exposure makes it possible to observe this area for tumors, which have occasionally given rise to this neuralgia Intracranial section prevents the recurrence of symptoms, which is possible following a peripheral section Adson believes that intracranial section is no more formidable than the neck dissection to reach the glossopharyngeal nerve The disadvantage of the peripheral section and avulsion is that the condition may recur, and secondly that the intracranial region cannot be visualized An alcohol injection is not feasible because of the small size of the nerve and its very close relation to the vagus, the jugular and the hypoglossal nerve It is remarkable that the patient following intracranial section of one glossopharyngeal nerve is not conscious of any paresthesia or discomfoit whatever from the loss of sensation of the nerve.

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RHINOLOGY

By O E VAN ALYEA, M D

THE COMMON COLD

Incidence—Ninety million work days are lost each year by U S citizens because of colds Since a common cold too often is a predisposing factor in more serious diseases, these estimates, based on studies by the $U\ S\ P\ H\ S$, have a considerable economic significance. among representative groups of people in every section of the U S, 15 per cent reported at least one cold a year; 30 per cent reported two colds yearly, 26 per cent suffered three colds annually; 14 per cent had four colds each year, and 14 per cent contracted five or more colds every year

A survey some years ago, established doubt as to the influence of climate on There were a the incidence of colds proportionate number of colds in Pasadena, Galveston and Chicago The fact was also established that colds were most frequent during sudden changes in temperature and humidity Kerr's experiments were carried on in an ideal environment (71° F-55 per cent humidity) He could not transmit infection ın a sıngle case

Susceptibility—The susceptibility of individuals to the common cold or influenza has been approached from various angles. Dietary errors or deficiencies, particularly of vitamins, have occupied the attention of some investigators. Others have concerned themselves with the theory that chronic sinuses act as reservoirs for storage of causative agents of cold epidemics. Many workers have attempted to lessen susceptibility by administering autogenous and stock vaccines.

- I G Spiesman and L Arnold¹ regard the vasomotor phenomena highly important in host susceptibility to common colds. They separate all individuals into three classes.
- 1 The normal resistant, one who rarely has a cold
 - 2 The chronic, frequent cold sufferer
- 3 The hypersensitive, noninfectious, allergic type

An investigation during the past three years of these two workers yielded the following results Thermal stimuli applied to the skin of a normal person causes definite vasomotor changes in the nasal mucosa Following an exposure to cold there is a sudden drop in the intranasal temperature with a vasomotor constriction and a bleaching of the This is followed by a gradual mucosa return to normal, although the stimulus has not been removed. The same test applied to the chronic cold type causes sluggish responses with considerable delay in readjustments Similar stimulation in the hypersensitive cases produced a syndrome of sneezing, itching, stuffiness, discharge and loss of the sense of The intranasal temperature changes were directly opposite to normal

Hydrotherapy consisting of hot then cold baths twice daily was found to be effective in increasing the vasomotor tone and this combined with a wheat free,

low carbohydrate diet were the two principal therapeutic measures used Mental hygiene, physical exercise and rest were important aids

Etiological Factors—R E Ashley² thinks that the common cold, in its early stages at least, is primarily a transient allergic manifestation. The purulent discharge which follows is due to the invasion of the tissues by a variety of bacteria superimposed on the vulnerable, allergically prepared mucous membrane

The allergic theory is substantiated by the nasal congestion with watery discharge from the nose and eyes, the sneezing, lack of fever, the marked increase in eosinophils in the stroma and secretion, absence of leukocytes, and absence of bacteria in the tissues

R L Cecil³ follows the trend of modern thought which credits the filtrable virus of Dochez with being the activating agent of the common cold and influenza. He says, "In view of the strides which have been made in the last few years it seems reasonable to conclude that within a short time we will have a fairly accurate conception of the etiology, pathogenesis and immunology of coryza and influenza"

Immunization—Evidence is already at hand that immunization against the influenza virus is feasible and effective. It seems quite likely that within the next few years some sort of combination vaccine, containing both virus and pathogenic bacteria, will be available for prophylactic purposes and that by the use of such a vaccine an active immunity against acute upper respiratory infections will be achieved.

Since 1921 vaccines have been reported as used in large series of cases with variable results. Thomson and Thompson state that a cold attack is less severe in those vaccinated. K. M. Houser⁴

vaccinated 108 students over a period of four years with these results:

| No relief in 21 per Relief in part or toto 79 per | |
|--|-------|
| Number of colds per year previous to injections | 479 |
| Number of colds per year after in- | 181 |
| Jections Number of days lost before injec- | 5 160 |
| Number of days lost after injections | |

Houser concludes that the incidence of colds is not materially decreased by the vaccine, but that the severity of the attack is, and he recommends its use Similar results were reached by M J Wallfield⁵ who administered vaccine to infants and children up to six years old, inmates of an infants' home

Oral vaccines have not as yet proven effective according to the J A M A 6 which states "In regarding an oral vaccine received as unacceptable, the Council on Pharmacy and Chemistry justified their action on the grounds that the reports of its use contained in the literature were insufficiently documented"

Therapy—A recent article by A G Rawlins,7 announces a new method of combating the action of the cold virus It is based purely on the theory that a similar virus which attacks plants has been successfully routed by treatment with sulfur dioxide fumes. In an epidenue, the author supplied 80 patients with this remedy and 66 reported themselves cured the first or second day When tried on colds of three or four days' standing it afforded no relief This last item fits in handily with the theory that after the third day of a cold the unknown virus ceases activity and the infection is carried on by the known bacteria Ephedrine combined with sodium amytal may be taken internally and, according to G H Gowen and A J

Nedzel⁸ affords considerable relief in the early stages of an acute cold

Local Therapy—Locally, your RE-VIEWER has found that ephedrine, one per cent in normal saline solution may be used effectively in all stages of a nasal infection Early, while the nose and throat are in a dry state, this solution prevents stasis by supplying the necessary moist medium for ciliary action and by its flushing action on accumulated micro-organisms and secretions this function is taken over by the excessive watery secretion supplied by the nose itself. Then, the ephedrine-saline solution is effective in minimizing the engorgement which is so apt to block ventilation of the sinuses and the breathing passages The most effective means of administering the ephedrine-saline solution is by instillation in the side posture, head-low position as described by Parkinson

A word of caution is sounded in the J A M A 10 concerning the too frequent use of oily nose drops. During the past three years many cases (usually in children under two years of age) have been reported of pneumonias due to aspiration of lipoid. Klinck stated that the fats and oils which cause this disease reach the alveoli of the lungs, where they collect and give rise to chronic inflammatory processes resulting in fibrosis. Lipoid pneumonia of the adult type, Ikeda says, is a distinct clinicopathologic entity. Liquid petrolatum is the chief etiologic agent.

At necropsy the lungs show evidence of the reaction of the tissues to a foreign body and the results of a secondary invasion by bacteria. Large amounts of oil are often present in the lung. Probably there are many cases of this disease other than the fatal ones that have been reported. The continued appearance of reports of fatal cases indicates the neces-

sity for greater care in the use of oily materials in the respiratory tract

A communication in the J A M A from L E Gaul¹¹ describes the present day local nasal therapy which consists of dousing the nasal ciliated mucosa with irritating chemicals and oils. He calls attention to the extensive use of mild silver proteins with the result increasing prevalence of cases of argyria. Fifteen new cases were reported in 1936, and this, no doubt, was only a small percentage of those which developed

SINUSES

Diagnosis—H R Slack, Jr, 12 points out that during the last few years the paranasal sinuses have been the subject of much discussion in medical literature All manner of therapeutic agents from diet to climate have been advocated for their treatment and a great many modifications of the generally accepted operative procedures have been recommended Many times the specialist is consulted about "sinus trouble" by patients coming of their own accord or referred by the family physician, when in reality the symptoms are caused by some general systemic disorder or certain local conditions entirely unrelated to the paranasal sinuses. There are too many mutilated nasal cavities that furmish an added source of irritation and tend to destroy the faith of the poor sufferer in the medical profession Before any therapeutic measures are instituted or operative procedures advised it is absolutely essential that the patient be given a thorough general medical examination and diagnostic study

In nine cases of fever, continuous or intermittent, over a period of a few weeks to a few years, the sinuses were overlooked as a possible cause A R Sohval and M L Som¹³ found this to

be due to lack of "sinus symptoms" and the presence of other conditions which were regarded as the cause of the fever

The diagnosis was usually established by roentgen study, nasal examination and diagnostic lavage. In most of the cases headache was present and the only symptom characteristic of sinus disease. In some of the cases the sinus involvement was slight and only discerned by irrigation. That this was the sole cause of the symptoms however, was shown by the relief of headache and the normal temperature following the lavage. The report of these cases points out the importance of consideration of the sinuses in the presence of fever of undetermined cause.

Treatment—An outline of his method of dealing with acute sinusitis in children is given by H Hays ¹⁴ Shrinkage and infrared radiation are employed Preparations containing vitamins A and D are given to build up general resistance When these simple treatments are ineffective a change of climate is often necessary

In adults the type of treatment to be employed depends upon the case. The general routine is to increase resistance and clean out the sinuses with a *suction douche apparatus*. Indications for surgery must of course be met when they present themselves.

The conservative viewpoint may be summarized as follows

- 1 The majority of sinus conditions acute or chronic will respond to conservative treatment
- 2 Too many antra are opened and washed out
- 3 In many cases, operative procedures on the sinuses will not result in permanent benefit
- 4 Treating sinuses with the suction douche apparatus will cure many cases and be of material benefit in others

5. The majority of serious conditions result from a lowered body resistance There can be no permanent improvement until the general system is brought up to par

A further plea for conservative therapy is made by S Stein 15 whose report deals with 143 cases of sinusitis in adults

These cases represented a variety of involvements from acute to the chronic, from the mild to the severe, with the accompanying complications. The symptoms of sinus infection vary with the type, the location, the number of sinuses involved, the presence or absence of complications, and the general condition of the patient. The treatment of sinuses should be directed towards ventilation and drainage. A plea is made for intelligent conservatism in our attitude towards sinus disease. Radical operations are not as numerous as they used to be

The conclusions arrived at are 1 A minimum amount of operative interference and trauma, 2, proper ventilation, 3, proper drainage of the sinuses This may be obtained through a skillful technic on the part of the surgeon who should have a thorough knowledge of the anatomy and physiology of the parts involved. The rôle of the turbinates and the septum should not be ignored There should be less need of extensive radical, either intranasal or extra nasal surgery, certainly much less than is being done There should be more attention paid to the after treatment of these cases, with more emphasis on physiotherapy, particularly heat, either through the use of 1, the infrared lamp, 2, diathermy in the chronic cases, 3, short wave diathermy

F Talia¹⁶ reports satisfactory results from the treatment of nasal or paranasal sinuses by **short waves** in chronic sinusitis. He used waves seven or eight meters long and Schliephake electrodes

of the condensing type in eight patients suffering from chronic maxillary, frontal or sphenoidal sinusitis. In chronic unilateral maxillary sinusitis the electrodes are placed over the sinus which is involved by the pathologic process and on the contralateral occipital region chronic bilateral maxillary sinusitis the classic occipitofrontal and bitemporal technics, respectively, are indicated When various sinuses are involved the treatment is given alternately to the different sinuses. The treatments are given daily or every other day, up to 30 or 40 during two or four months Each treatment lasts for 15 minutes during the first month or two months and for 30 minutes (and rarely for 40 minutes) during the last months. The treatment is discontinued for ten days at given intervals According to the author the treatment is of value especially in chronic sinusitis of short duration Maxillary sinusitis, especially of the inflammatory and suppurative forms, responds to the treatment better than other forms of chronic sinusitis

During the 12 years since its origin the A W Proetz¹⁷ technic of introducing fluids into the sinuses has gained considerable vogue both in this country and abroad Proetz reviews the literature, evaluates the method and adds his comments to the various phases of its use, such as, technic, solutions used, treatment, radiography and interpretation and diagnoses

For proper displacement filling of a sinus, four prerequisites are 1, the ostium must be in proper position relation to the sinus, 2, the ostium must be covered by the fluid, 3, negative pressure must exist at the ostium and 4, the ostium must be patent

In treatment of sinus disease by this form of instillation various drugs and combinations of drugs have been used.

Ephedrine 0 25 per cent in normal saline solution has proven the most effective.

When sinuses do not admit fluids it is usually a surgical indication

When solution passes in and out of the ostium a sinus may be thoroughly irrigated and its contents studied The first washing usually removes a single large opaque vellow lump In the second washing there are present several similar lumps, though smaller and ropey in appearance The third or fourth washing brings forth a few curds and the next irrigation appears clear but is in reality heavy mucus Treatment should continue until this mucus has disap-Solutions containing various preparations of bacterial antigens, lysates, polyvalent antivirus and bacteriophage have been instilled into the sinuses by the displacement method with a fair measure of success

The instillation of radiopaque oil by this method aids in the interpretation of roentgenograms of the sinuses. This applies especially to the small ethmoid cells and to sphenoids which are so variable in anatomy and relationship and so apt to encroach on each other and on adjacent structures.

ASTHMA

Treatment—N Fox and J W Harned¹⁸ outlined their surgical and non-surgical treatment of asthma as carried out by them in a series of cases over several years. Their efforts have been directed in the main toward relief of the bacterial or infectious type of asthma. They feel that the rhinologist at best can merely aid in clearing up infection which occurs so readily in asthmatic persons, whether it is the cause of the asthma or merely a contributing factor. Their procedure in brief is Admission of patient to the Department of

Allergy Careful history and complete examination including cutaneous tests and roentgen study of the chest Examination in the department of otolaryngology where surgical procedures such as sinus irrigation and removal of polypi are immediately instituted.

Patients negative to all allergens, except bacteria, are treated in this department with non-specific proteins, the others being returned to the department of allergy for desensitization Surgical treatment when indicated is radical. In the suppurative cases only the sinuses involved are operated on, whereas, those with hyperplastic tissue receive a complete exenteration of all sinuses.

The authors report a 60 per cent cure in the 40 cases of this later group, 45 per cent were clinically cured in those patients receiving bilateral ethnioidectomy and antrum operations. Those receiving ethmoidectomy alone were relieved of symptoms in 33 per cent while 60 per cent obtained a five-year cure after operations on one or both infected maxillary sinuses. Failures were attributed to faulty allergic tests, changes in a patient's allergic status and secondary suppuration and polyposis of the frontal sinuses.

The non-surgical treatment was given to 150 patients, called border line cases, those whose nasal conditions did not warrant surgical intervention. Included with this group were children, patients over 50 and all poor operative risks. They received various chest injections of poppy seed oil, and autogenous antivirus, intramuscular injections of treated tissue for asthmatic patients, convalescent serum from asthmatics, and radon implants. The results were only temporary in most cases, but even this is preferable to entire neglect or to surgery when it is not indicated.

NASAL ALLERGY

Diagnosis—Hypersensitiveness is not difficult to diagnose according to L Unger¹⁹ for there is apt to be an associated allergic manifestation such as a history of eczema or positive family history, both helpful points. As further diagnostic measures we have skin tests and the eosinophile count in the secretions from the eyes, nose and bronchical tubes

Treatment—Nasal surgery in allergic individuals is indicated only for severe infections or obstructions. The best treatment for hay fever, according to Unger, seems to be injections of pollen extracts. He uses large doses and follows the perennial method of treatment.

Specific immunization according to A R Hollender²⁰ should be tried in every case in which the offending allergen can be demonstrated, or at least it should be kept from contact with the patient whenever at all possible Whenever surgical intervention is indicated, it should be resorted to, for the tendency to avoid nasal or sinus operations in the presence of vasomotor rhinitis is fallacious Of all non-specific methods of treatment which have been employed in vasomotor thinitis, zinc ionization has proved clinically very valuable as a palliative of prolonged effectiveness and possesses definite advantages over other procedures Hollender believes that while iontophoreses is only occasionally of benefit in seasonal hay fever and asthma, it merits a trial, especially after other means of therapy have failed to produce

In treatment of cases of nasal allergy as much attention must be paid to foods as to inhalants, according to H J Rinkel ²¹ In diagnosis he depends upon skin tests, clinical studies and the leukopenic index, which, although difficult to carry out, is about 81 per cent accurate.

L W Dean and others²² and his coworkers completed a 20 month study on various forms of therapy in chronic vasomotor rhinitis Considering the deleterious effects of zinc ionization on the nasal mucosa a search was made for other remedies equally efficient The agents tried were radium, diathermy. trichloracetic acid, the actual cautery. alcohol and phenol. No method proved highly satisfactory A careful study of the patient is essential. Dietary defects and endocrine disturbances should be corrected and infection eradicated Avoidance of allergens, desensitization and operative procedures are important in the proper handling of a case

A similar viewpoint concerning ionization is expressed by A M Alden²³ who points out that ionization in no way alters the fundamental physiologic characteristics of the individual which make him allergic and that it even decreases for only a relatively short time the ability of the nasal cells to combine with and be affected by their offending allergens What it does is, by a mechanical change, to render the nasal mucosa less able to produce disagreeable obstructive and secretory symptoms in response to either external irritation or vasomotor stimuli Desensitization is still method of choice in the treatment of this condition, ionization being reserved for patients in whom the obstructive and secretory symptoms are predominant and in whom the mechanical relief to be expected is more than commensurate with the tissue damage incident to the ionization Asthma has not been lessened after ionization except in a few cases, in which the author is sure that the improvement was due to the relief from nasal obstruction rather than to any change which the treatment brought about in the status of the patient

C. A Hutchinson²⁴ advocates injections of *sclerosing agents* for permanent shrinkage of the turbinate in preference to cautery. He uses 30 per cent *carbolic in paraffin*, producing scarring in the deeper layers of the mucosa and submucosa without injury to the ciliated epithelium. One injection is sufficient and produces excellent results

Ethmosplenofrontal Operation—Radical or complete sinus surgery seems indicated in certain cases when partial operations have failed. The technic of the ethmosplenofrontal operation changes very little from year to year W L Simpson²⁵ describes his operation which has proven satisfactory in a large number of cases

Cristectomy — Intranasal window operations have been described at various times since Canfield's article published in 1908 J H Childrey's technic²⁶ includes removal of the pyriform crest, which he deems important for the success of the operation

Although many articles have appeared in the literature during the past few years showing the excellent results obtained from antrostomy, rhinology has failed to give it the full measure of its worth. The Caldwell-Luc operation is still the method practiced by many rhinologists even though the simpler intranasal operation would often suffice. The advantages claimed for cristectomy are that it is a simple office procedure, a very good view is obtained of the antrum and its contents may be removed through this opening if so desired.

SINUS DISEASE

Complications — Extension of Infection to Orbit—L Hubert²⁷ points out that orbital infections due to nasal sinusitis may extend into the orbits by direct extension from the diseased bony

wall: which separated these sinuses from the orbital cavities, and by the venous blood stream, i e., by a phlebitis of the veins of the various sinuses, which anastomose with the superior and inferior ophthalmic veins that supply the fatty cellular tissue of the orbits All orbital infections can be classified in the following groups: (1) Inflammatory edema of the eyelids with or without edema of the orbit, (2) subperiosteal abscess with (a) edema of the lids and orbit, (b) spreading of the pus to the lids (erroneously called orbital abscesses), (3) orbital abscesses. (4) severe and mild orbital cellulitis, and (5) septic and aseptic, (6) cavernous sinus thrombosis In the first group the infection is confined to the nasal sinuses and there is only an inflammatory edema of the lids, which may become markedly swollen Thirty-one patients belonging to the first group were admitted to the hospital as bed patients Of these, 20 were successfully treated symptomatically, one had a lid incised, one had the middle turbinate removed and nine had external radical operations There were five deaths in this group In the second group the infection involves the bony wall and the periosteum and a collection of pus forms between them There were 46 such cases, in nine of which the pus was confined between the bone and the periosteum and in 37 the pus involved the lids All recovered after surgical treatment The infection in the third group spreads into the orbital tissue proper either through the orbital wall and fascia or through the venous circulation 22 patients, two died of meningitis and one of a brain abscess. In the fourth group the infection extends into the orbital tissues through the venous circulation, causing a phlebitis of the ophthalmic veins. Nine patients had severe orbital cellulitis, six of whom died of

meningitis. There were two patients with a mild orbital cellulitis following a nasal infection They were discharged cured after a few days of local treatment. In the fifth group the infection had extended from the ophthalmic veins or directly from the sphenoid sinus into the cavernous sinus. It is almost impossible to distinguish clinically such an orbital cellulitis from a cavernous sinus thrombosis, unless it is accompanied by an edema over the mastoid emissary The difficulty in the clinical diagnosis is due to the fact that signs which are supposed to be characteristic of it are not due to a thrombosis of the cavernous sinus alone but to a phlebitis of the ophthalmic veins Both of the two cases of septic cavernous sinus thrombosis were fatal. The two patients who recovered were diagnosed as having aseptic cavernous sinus thrombosis The diagnosis is, of course, doubtful

Extension of Infection to Chest-Infections tend to pass from the upper to the lower part of the respiratory tract rather than in the reverse direction. This tendency is, according to M Settel²⁸ (1) Aspiration of secretions with their bacterial products, by gravity and suction, (2) muscular action in the pharynx, as in swallowing, hawking, (3) ciliary action in the upper and lower part of the respiratory tract except in the middle and lower parts of the pharynx, where the epithelium is of the stratified squamous variety due to digestive function, (4) neurogenic tonus of the sympathetic and parasympathetic systems, both of which supply the organs of respiration, and (5) vascular and lymphatic pathways for the spread of infection The evidence that certain disorders of the lower part of the respiratory tract, notably chronic nontuberculous bronchitis, bronchiectasis and bronchial asthma, have followed this sequence from the upper part of the respiratory tract is based on a number of observed facts that make it seem conclusive · (1) The same pathogenic organisms are found in the primary foci as in the metastatic lesion of the lower part of the respiratory tract. (2) Disorders of the lower part of the respiratory tract have repeatedly improved and in many cases been entirely cured after the infection in a sinus has been cleared up by suitable treatment. The rapidity with which this change takes place after eradication in a sinus infection argues strongly in favor of such a sequence (3) It may be possible to prove that an infection has come down from the upper part of the respiratory tract to the lower, by moculating into animals the pathogenic organisms obtained from smears of the nose and sinuses, on the one hand, and from the sputum, on the other, and then comparing the results (4) The frequency with which an infectious disease is found to exist simultaneously in the lower and upper parts of the respiratory tract cannot be regarded as an accident but is evidence that an infection at work in one locale has sent its emissaries, as it were, to found a colony in another region

Intracranial Complications—Intracranial complications in accessory sinus disease occurred in 36 out of 1330 patients or in about three per cent of the cases according to Gunnai Hagerup ²⁹ Of these cases three followed operation and one case traumatic frontal sinusitis

Among the 33 cases of spontaneous origin there were 14 cases of leptomeningitis of subdural abscess, 12 of cerebral abscess, four of pachymeningitis and extradural abscesses, and three of cavernous sinus thrombosis. At the Municipal Hospital in Copenhagen the number of cases of suppurative otitis and of inflammations of accessory sinuses has for

a long series of years been distributed in the ratio of seven to one

The intracranial complications must in 20 cases be presumed to have originated from the frontal sinus, in nine from the ethmoid cells and in three from the sphenoid sinus There were no cases of intracranial complications originating from the maxillary sinus On the basis of this material it is concluded that when a pleocytosis has developed, radical evacuation of the primary focus and exploratory exposure of the dura are indicated If a pachymeningitis is found it is widely exposed until it is seen to be surrounded by sound dura Cerebral puncture may also be indicated

Osteomyelitis—H C Behrens³⁰ describes two types of osteomyelitis: the localized, which results from a small perforation due to pressure of pus in a frontal sinus, and the rapidly spreading, which results from sudden change in activity of the localized type Mortality is high, ranging from 35 per cent to 79 per cent Those developing postoperatively are more serious than the spontaneous type Conservative treatment lessens the mortality, and the presence of streptococcus raises the mortality. As a possible prophylaxis all infected sinuses must be drained, the curette should never be used forcibly on the walls, the periostium is to be preserved and rasps should not be used Swimming with chilling of the body should be forbidden patients who have chronic sinusitis The treatment ranges from radical to conservative, the radical calling for thorough and wide removal of all diseased bone, draining of all abscesses and grooving through healthy bone an inch beyond the disease The conservative treatment calls for removal of sequestrum as they are found with the addition of transfusion and supportive treatment

H L Williams and F. R Heilman³¹ describe three clinical types of the disease: the fulminating type, the localizing type, and the spreading type. In four cases of the fulminating type all died from meningitis which developed during the first 24 hours after the first symptom of sinusitis There were three cases of the localizing type In these, after a long interval, the sequestrum was lifted out and healing resulted. In their six cases of spreading type there were two deaths and four recoveries They usually wait for a possible tendency to localization If there is no sign of such, they operate using the Furstenberg technic If this fails a complete radical is instituted All diseased bone is eradicated well beyond the apparent limits Brain abscesses are drained through clean fields in the anterior temporal region and as a therapeutic measure they use a daily irrigation with an autogenous anti-virus solution This proved effective in two cases where the invading organism was an anaerobic streptococcus While waiting for the preparation for this antivirus they institute similar irrigations with Rosenow's concentrated hyperimmune polyvalent antistreptococci serum in the normal saline solution

The authors feel that the inflammatory change in the dura is the best guide as to surgical removal of bone and feel that diseased bone should be dealt with before treating the complications. This is due to the work of Furstenberg and Mosher who have demonstrated that propagation of the disease is by thrombosis of the dural veins which communicate with the dural sinuses and intradural veins.

A W Adson and B E Hempstead³² mention four important surgical principles which should be observed in handling osteomyelitis (1) Adequate drainage of the frontal sinus. (2) Re-

moval of pus, necrotic bone and all adjacent white dead bone (3) Preservation of periosteum. (4) Hair line incision

Their technic calls for obliteration of the frontal sinus by removing its inner plate. The cavity is filled with gauze saturated in iodine which is removed on the third day

L. J Lawson³³ reports two cases of osteomyelitis of the sphenoid bone, one of which was produced by extension from petrositis and one by reactivation of an old infection of the sphenoid sinus In the first case an unusual amount of destruction of the sphenoid body developed before the onset of diffuse fatal In the second case hasal meningitis neither meningitis nor thrombosis of the cavernous sinus, which are the more usual complications, developed, but the process took the unusual outlet of posterior cervical thrombophlebitis, with abscess formation and late septicemia

The development of recurrent asthma with the onset of infection of the sphenoid suggests that previous disease of the sphenoid may have escaped notice and that its reactivation due to lowering of the patient's resistance by the mastoid infection caused the unusual symptoms and overwhelming infection which followed Osteomyelitis of the sphenoid bone will not respond to drainage by steel drills. It requires extensive surgical removal of bone beyond infected thrombosed blood vessels as in other This is not possible by any locations present day technic

Osteomyelitis Therapy—The picric acid-calcium carbonate therapy of Stewart is used in cases of osteomyelitis as a substitute for the maggot treatment. It has been found by Stewart that maggots exude calcium carbonate, and by Bechold that calcium ions stimulate phagocytoses. It is also known the

bacteria excrete leukocidin which destroys phagocytes A dilute aqueous solution of *picric acid* renders the leukocidin inert

Stewart's therapy consists of the use of the two solutions (1) 025 per cent acqueous solution in distilled water with eight per cent glycerine content (2) A calcium carbonate suspension in distilled water

H J Gray³⁴ has used this solution irrigating chronic antrums with or without an associated bone involvement with good results. He first sprays in the picric acid solution and follows it with the calcium suspension. Progress was marked and rapid. Treatment is given daily until the infection is cleared up

Hyperostosis—M Raso³⁵ performed necropsies in 13 cases of hyperostosis of the internal aspect of the frontal bone (Morgagni syndrome). Although this condition may be attributed to many causes Raso believes that local inflammation, secondary to that of the paranasal pneumatic cavities, and local circulatory disturbances are the most plausible etiopathogenic factors.

CRIBRIFORM PLATE FRACTURE

Fractures of the cubriform plate are usually associated with dural lacerations. This, according to H. Cairns, 36 may be expected because over this bone the dura is its thinnest and it is, moreover, closely adherent by its extensions through the bone along the olfactory nerves. With these fractures there is usually a discharge of cerebrospinal fluid into the nose with danger of intracranial infection.

Fractures of the cribriform plate occur often in accidents of the "head on" type, especially in aeroplane accidents, where considerable force strikes the facial bones and spreads backward along the base of the skull

Of lesser importance are fractures of the frontal sinus. When cerebrospinal rhinorrhea is present with frontal fractures the dural tear is due to a concurrent fracture of the cribriform plate. When this plate is fractured there is the possibility of the formation of an aerocele due to sneezing or to blowing the nose. Delayed complications often follow head injuries and may appear at any time from a few weeks to two or three years following an apparent recovery. The attack comes suddenly with a head cold of an acute sinusitis.

Injury to the cribriform plate and dura may occur during intranasal operations and often terminates fatally. The possibility of early repair is considered in these cases

Another group of cerebrospinal rhinorrheas are classified as the spontaneous type. An etiological factor may be some congenital deficiency of the cribriform plate or (a) hydrocephalus with slow growing intracianial tumor, (b) frontal and ethinoidal osteomas and (c) pitutary tumor. Injuries of the sphenoid sinus may account for still another group of these cases. The escaping fluid comes from the superior meatus and there may be no loss in the sense of smell, whereas it is usually lost in ethinoidal injuries

C Coleman³⁷ concurs in the ideas expressed by Cairns concerning the handling of cribriform fractures. He thinks dural lacerations should be repaired if the cerebrospinal leak exists for three or more days after injury, provided, of course, the patient's condition permits. This may be done through a small frontal flap with elevation of the dura from the floor of the fossa exposing the inner wall of the frontal and the ethmoid area. Injuries involving the external plate of the frontal sinus alone.

are usually treated by simply suturing the skin wound Depressed fragments when extensive are, of course, elevated before closure.

FACIAL INJURIES

Facial injuries from automobile accidents are now of common occurrence C L Straith³⁸ suggests several principles which may well be observed Avoid overtreatment, rough handling, manipulations during shock, etc., (2) cleanliness, a simple clean compress over a lacerated area controls bleding and prevents further contamination, (3) repair of wounds should only be undertaken in ideal surroundings with proper equipment Foreign material must be carefully removed and ragged edges trimmed before suturing In severe crushing injuries, depressed bones and fragments are replaced and held by wires and splits Skin losses if small can be restored at once by grafts taken from the upper lid or from behind the ear Larger losses are replaced later by pedicle grafts

INFECTIONS OF THE FACE

Etiology — U Maes³⁰ reviews 20 fatal cases of infections of the face. He regards the dangerous area to be the triangle which extends from the angles of the mouth to the bridge of the nose. The vulnerability of this area is due to the thinness of the skin and its constant exposure to trauma, the rich vascular supply with its direct passage to the cranium, the preponderance of connective tissue which adapts itself poorly to infection, the constant motion of the lips which prevents localization.

The infectious agent is usually the staphylococcus aureus. When trauma is introduced, the infection spreads rapidly

by way of the rich vascular supply producing thrombophlebitis, thrombosis of the cavernous sinus, massive blood stream infection, meningitis and metastatic abscesses. The course of the disease is brief and characteristic. The symptoms and signs after this stage include severe pains, chills, hyperpyrexia, delirium or coma and prompt death

Treatment—The general opinion now held is that conservative measures, chiefly absolute rest of the parts, warm compresses, and supportive measures, give the best results, while surgical incision gives the worst

HEADACHES

Types—Headaches of nasal origin are classified by T Burgess⁴⁰ as follows (1) Those associated with suppurative sinus infection, (2) those associated with nonsuppurative or hyperplastic sinuses, (3) those without any involvement of the sinuses. The latter group may be further subdivided into vacuum headaches, and the neuralgias

Diagnosis—Suppurative sinus headaches are easily diagnosed and caused probably by the pressure of enclosed pus Frontal, anterior ethnicid, and maxillary sinuses produce pain above the eye on the involved side. Posterior ethnicid, and sphenoid produce pain in the parietal and occipital regions. Acute sinusitis is accompanied by tenderness to pressure over the involved sinus. Usually there is no tenderness in chronic cases.

Hyperplastic ethmoiditis and sphenoiditis produce pain in the neuralgic type from involvement of the contiguous nerve trunks. It is usually located in the temporal and occipital region, occasionally frontal

Vacuum headaches are due to some obstruction interfering with the free exchange of air between the nose and sinus

It is most common for the frontal sinus, but has been described for an anterior ethmoid. The sinus itself is normal. It may be due simply to subacute swelling of the mucous membrane about the ostium of a sinus, or it may be due to a deviated septum, enlarged middle turbinate, or hypertrophied uncinate process. Relieving the obstruction cures the headache.

Neuralgias are those of the supraorbital, anterior nasal, and infraorbital nerve, and the sphenopalatine ganglion syndrome

Headaches have also been ascribed to involvement of the vidian nerve sphenopalatine syndrome is due to involvement of the sphenopalatine ganglion, which is a very important nervous structure located just lateral to the mucous membrane behind the posterior tip of each middle turbinate. In both of these conditions, headache is located on the side and back of the head and never across the midline Therapeutic test is an application of cocame to the region of the nerve structure, which should result in prompt relief of the headache Treatment consists in application of drugs of this region, or alcohol injection of the nervous structure

Sluder Syndrome—The Sluder syndrome is caused by diseased antrums more often than is usually suspected In this condition there is a pain at the root of the nose, in the lower jaw and teeth, sometimes also the ear, back of the mastoid occiput and neck, and in severe cases extending to the aim, forearm, hand and In searching for the even fingertips cause of persistent headaches, it is well to remember that there are various kinds of headache and that in a given case two or more types may be intermixed; that a general physical examination having already been made, the following causes must be considered (a) Allergy, (b)

psychalgian, (c) the endocrine; (d) the teeth, (e) sphenopalatine ganglion hvpersensitiveness, and (f) errors of refraction and muscle imbalance The Sluder syndrome has been attributed to various factors by different authors, but Tilley implicates the antrum of Highmore, and it is elaboration of the thought expressed by Tilley that the present report is mainly concerned C B William's41 report is based upon 211 patients (315 antrums) operated upon during the past five years by the simple window method Headache was classified as to types as Lower-half, generalized, vacuum frontal and mi-Complete relief in this report means freedom from symptoms from nine months to four years In conclusion the authors holds that more cases of the Sluder syndrome are directly traceable to diseased antrums than has heretofore been recognized, 315 per cent in the present series

Migraine — T J C von Storch42 suggests that, in reporting cases of migrame, utilization be made of the four cardinal components of the syndrome Recurrent headache, preferable but not necessarily hemicranial in type, associated visual symptoms, classically scintillating scotomas, temporary gastrointestinal phenomena, usually nausea or vomiting, and hereditary migraine diatheses, occasionally an epileptic history No single pathologic process nor its presumed mechanism will explain conditions observed in an entire group. On the other hand, any one of the allergic, colonic, endocrine, duodenal hereditary or psychic processes may be the primary factor in certain cases In other words, each etiologic factor appears to be reasonable for a selected group, but none for an entire series It would seem, therefore, that the underlying pathogenesis of the migraine A mechanism syndrome is multiple which may be common to all types of

migraine is dilatation of the dural and possibly temporal arteries, with consequent stimulation of their periarterial plexuses. This seems to be the only mechanism related to the common symptom headache *Ergotamine tartrate* is the most efficient nonsedative means of aborting or terminating individual attacks of migraine Prevention of the attacks depends on determination of the underlying pathologic condition present in each individual case

H. H Burnham⁴³ attributes the cause of "constitutional or migraine" headache to be nasal in origin. His conclusions are based on Lewis' work in the metabolites. These are irritants formed in the tissues which cause dilatation of minute blood vessels, which in turn cause disturbances in the neurovascular mechanism and sensory nerves. Such substances may be produced in the nasal mucosa by bacterial toxins or exposure of the individual to sudden thermal changes.

The headache or pain which results involves branches of the trigeminal nerve Two areas commonly affected are the anterior tip of the middle turbinate supplied by the anterior ethmoid and a point just under the bridge of the nose, over the course of the lateral nasal nerve, a branch of the anterior ethmoid

The typical attacks begins during a cold in the head with a pain between the eyes and in the frontal region. This extends over the temporal, parietal and vertical areas following the distribution of the ophthalmic division of the trigeminus. The pain is usually limited to one side, but in severe cases, may involve both sides. With the headache the patient is tired but rest does not relieve the condition, nor do the usual headache remedies.

The nasal and sinus examination reveal no abnormal state. The diagnosis is established and relief afforded the

patient by the simple extremity of applying ephedrine solution to the sensitive areas in the nose

THE NASAL SINUSES

Malignant Growths

F L Lederer44 believes that a malignant neoplasm of a nasal sinus is seldom if ever confined within a mathematically calculable area By virtue of the characteristically slow growth of a neoplasm within a bony cavity, it is observed as such at a time when it falls within the classification of inoperability, that is, when the diagnosis finally becomes self evident Unfortunately, inspection, aus cultation and palpation, anterior and posterior rhinoscopy, endoscopy, transillumination, roentgen examination and biopsy do not always facilitate a conclusive diagnosis in early cases Furthermore, confusing clinical pictures are produced by intercurrent or coexisting diseases, particularly by those which cause swellings about the maxilla and orbit Syphilis and tuberculosis may obscure the diagnosis of cancer, thereby delaying proper therapy Peculiar histologic responses of the various tissues to tumor growth and infection may also hinder a correct diagnosis

The development of sinus cancer 15 slow, metastasizing infrequently. There is a definite tendency of such tumors to invade the meninges and other intracramal structures. While the symptoms usually vary, in the main the points to be noted are unilateral nasal obstruction, mucopurulent or serosanguineous discharge, headaches (usually frontal), nasal hemorrhage, fector, cranial nerve involvement consisting of sensory disturbances (neuralgic-like pains, paresthesia and anesthesia), ocular disturbances (proptosis, limitation of motion, papil-

litis and atrophy), olfactory disturbances (anosmia and parosmia) and external deformity Surgery, electrosurgery and irradiation combined have given fair results in malignant tumors of the nasal sinuses, especially those of the antrum, in spite of the fact that 80 per cent have been termed inoperable, because of invasion of vital structures Malignant growths of the frontal sinus if seen in time may be operable, in which case the sinus should be exposed widely through the external route Cosmetic results should not enter into consideration As much of the mass is removed as is possible and the remainder is coagulated by surgical diathermy If the dura is invaded, the frontal lobe is to be exposed fully The skin flaps are sutured to one side and the wound is left wide open for contact radium applications Radium may be used in this region with impunity because the dura is quite resistant

SADDLE NOSE

Syphilis contributes to the causation of a saddle deformity which rarely occurs without trauma, except in the congenital types M M Wolfe⁴⁵ examined 3000 inmates of a penitentiary and served many saddle deformities thinks the incidence of syphilis among patients with all types of saddle deformities is very low Infections, the granulomatas and other diseases, by their instructive processes, are capable of producing a saddle nose, but the number of such cases is small. Trauma is by far the most etiologic factor capable of producing a saddle nose

It is advisable not to undertake the correction of saddle nose when the patient's Wassermann reaction is positive. If the blood remains persistently positive in spite of adequate treatment, the

operation may be undertaken, but with greater danger

SPHENOID SINUS

Anatomy — A study of 1600 skulls made by F W. Dixon46 supplied valuable data concerning the sphenoid sinus and its adjacent anatomy The extreme variations of this cavity were noted, its measurements were recorded and a study was made of the ostium sphenoidal The close approximation of such structures as the optic canal, the vidian canal, and the internal carotid artery were not uncommon findings The ostium was usually found in the upper mesial fourth on the anterior surface The bony foramen was round or oval, there being twice as many round as oval openings The average diameter of the round opening was 5 03 mm, the oval 42 mm by 58 mm. The average distance from the septum to the center of the ostium was 49 mm and its distance from the cribrifoim plate was The ostium usually faced 8 25 mm toward the tip of the nose although if the sinus was large and encroaching on the posterior ethmoid the ostium faced toward the septum and on occasions faced upward. In the nonmacerated skulls the membranous ostium was noted to be quite small and maccessible surgically. It could be penetrated easily and the same applied to the thin anterior wall of the sphenoid Attention is called to the over-11ding of the sphenoid by posterior ethmoid cells which happened in 55 cases Hence in cases of optic neuritis this cell must be considered as well as the sphenoid

FRONTAL BONE

Ossification—V T Imman and J B de C M Saunders⁴⁷ give a historical review of the literature on the ossification of the frontal bone and its accessory

centers Observations were made on a total of 98 fetal skulls ranging in age from the sixth week of intrauterine life to the tenth month after birth Primary centers of the frontal bone made their appearance in the superciliary region. No secondary centers of ossification have been found at any time in the frontal bone The changes that have given rise to the error that such centers exist are Attempts that have been considered made to homologize portions of the frontal bone with the prefrontal and postfrontal elements of premammalian skulls have been based on the presumed existence of secondary centers. As no such centers exist in the human skull, conclusions drawn on this basis must be discarded

ABSORPTION THROUGH OLFACTORY MUCOSA

That disease viruses and pigment may be readily absorbed through the olfactory mucosa is shown by G Rake,48 who observed that prussian blue particles pass rapidly from the surface of the membrane and within two minutes are found in the tissue spaces, in the blood and lymph vessels, in the perineural spaces of the olfactory nerve fibers and in the subarachnoid space and piaarachnoid membrane Preliminary treatment of the olfactory mucosa with tannic acid does not alter the speed with which this absorption occurs It does, however, cause the inflammation of the mucosa and appears to prevent the pigment from entering the olfactory sensory cells Both pneumococci and Salmonella enteritid pass through the olfactory mucosa and reach the tissue spaces, the vessels and subarachnoid space with the same rapid-They invade by ity as the pigment passage between the cells of the mucosa and there is no apparent affinity of the organisms for the olfactory sensory cells. Tannic acid treatment of the olfactory mucosa in no way alters this invasion of organisms through the mucosa. The pantropic virus, equine encephalomyelitis, was detected in the forebrain as promptly as were pigment and bacteria, neurotropic viruses, however—those of St Louis encephalitis and rabies—were not demonstrated in less than 24 hours

Zinc Sulfate Prophylaxis in Poliomyelitis—The successful use of a zinc sulfate spray in the prevention of experimental poliomyelitis in monkeys has recently stimulated much activity in its application to the human

E W Schultz and L P Gebhardt⁴⁹ reported the results of extensive investigation with 40 chemical concentrations of zinc sulfate in solution. The final choice of this drug for trial in human beings was due to its surprisingly high protective action in monkeys, its low toxicity and its simple composition.

In view of the findings of Shultz, M Peet, D H Echols and H J Richter⁵⁰ outline a technic for the application of this immunizing agent in humans. They recommend the use of zinc sulfate, one per cent, pontocaine (local anesthetic), one per cent in 0.5 per cent sodium chloride. One cc of this solution is instilled (Proetz position) or sprayed over the olfactory area of each side of the nose. The procedure may be repeated at intervals of two weeks.

Diasagreeable symptoms, such as anosmia, headache, sneezing and burning sensation in the nose may follow the instillation, especially in the adult, but they are transient only, and as far as is known no permanent damage will result

Peet's technic with variations was given an extensive trial during the 1937 epidemic of the disease Immunizing centers were established in various cities

throughout this country and Canada where large groups of children were treated and records kept. To date, no definite conclusions may be drawn as to the value of the method

NASAL SEPTUM

Deviated Septal Cartilage

L A Peer⁵¹ has devised an operation for those cases wherein there is a marked deviation of the columella cartilage into one nostril. This is done at the time of a submucous resection of the septum and consists of substitution of a strip of the septal cartilage for the displacement segment. This strip rests between the nasal spine and the tip of the nose extending back to the upper beam of cartilage. Mattress sutures hold it in place and prevent bleeding. The results are good in that this cartilage serves as a permanent support to the nasal tip.

Septal Ulcers

In March, 1936, M H Barsky⁵² saw two employees of a copperplating establishment reporting for treatment of infected abrasions and acute coryza They volunteered the statement that many of their coworkers suffered from similar complaints Examination revealed the presence of shallow ulcerations of the nasal septum and turbinates As a result of these observations, all employees of the plating department of this establishment were examined and a hygienic study of the premises was conducted The disturbance was effectively corrected There were no recurrences of the difficulties in the old workers, nor did any appear in the new employees The direct causes of the disturbance were improper control of baths, failure to exhaust the spray thus produced and inadequate general ventilation

ATROPHIC RHINITIS

Little headway has been made in the treatment of atrophic rhinitis, although many new forms of therapy are constantly being tried. A method which proved to be of temporary aid only was tried in Poland by A Zakrazewski and J Wiza 53 Ozena was treated by filtrates containing the specific bacteriophages of the organisms found in the nasal cavities of the patients

In ozena and, to a lesser extent in atrophic rhinitis, there is endarteritis with narrowing of the blood vessels and a diminution of the blood supply. J S Stovin⁵⁴ applied *mecholyl* (acetylbetamethycholine chloride), a peripheral vascular dilator, by *iontophoresis* in the nose, in a series of cases Treatments are given three times a week until improvement. The ozena cases lose their foul odor and the simple atrophic cases have a return of the sense of smell. A similar result was noticed following the use of *normal saline solution* as a medium instead of mecholyl

CHOANAL ATRESIA

Attention is called to the gravity of congenital bilateral choanal atresia B N Colver⁵⁵ thinks this condition has undoubtedly been the unsuspected cause of many deaths in the newborn. He advocates early operation in the complete atresia, but thinks operation on the unilateral type may be deferred until the child is several years old. The operation is performed under general anesthesia, the bony obstruction being removed by a gouge, burn or rasp. A good result depends upon removal of the posterior portion of the nasal septum

H B Lemere⁵⁶ operated on a twomonth-old infant suffering from a bilateral atresia with satisfactory results A curette was used to force a passage through the membrane Following this procedure on one side, the child immediately closed its mouth and began nasal breathings

C. M Anderson⁵⁷ reports one bilateral and five unilateral cases, the total number seen at the Mayo Clinic since 1907. They were all operated on with good results.

Several interesting facts were brought out by these three papers and the discussion of them, to wit (1) The importance of an early operation on the newborn in case of bilateral involvement, (2) importance of postnatal examinations of patients preceding adenoid and septum operations, (3) a good result may be expected if a large opening is made and kept patent, (4) there are usually no hearing defects on the affected side, which causes one to question the necessity of septal resection in deafness cases, (5) the nasal sinuses are fully developed and unaffected on the occluded side which should upset the theory of Freis, that the development of the sinsues is contingent upon the presence of air currents in the nose, (6) the nasal mucosa in the olfactory area on the blocked side shows almost complete desquammation of the surface epithelium and fibrous thickening of the submucous tissue This is in line with the modern conception that respiratory sequence is necessary for the maintenance of normal nasal mucosa

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LARYNGOLOGY AND DISEASES OF THE NECK

By Louis Zolo Fishman, MD, MS

LARYNX AND TRACHEA

Congenital Abnormalities

An interesting factor in speech disturbances is presented in the case of "Laryngoptosis" reported by G Tucker 1 Traction exerted upon the hyoid bone by a tight band of fibrous and muscular

tissue, representing a unilateral congenital abnormality of the sternohyoid and sternothyroid muscles (left side), served to displace downward all of the structures attached to the hyoid from above (chin, tongue, epiglottis, etc.) and to the larynx from below (trachea and bronchi) The effects were an inability to close the mouth in extension of the neck and an inability to protrude the tongue beyond the margins of the teeth; the hvoid bone was pulled down to just above the suprasternal notch and the left main bronchus was distorted so that it came off the trachea more nearly at a right angle than normal No angulation of the trachea itself was apparent. Resection of a small part of the band of tissue was immediately followed by the ascent of the hyoid bone and larynx to their normal positions, the tongue could be readily protruded beyond the teeth, the head could be thrown backward without the necessity of opening the mouth: articulation became clearer than theretofore

Foreign Body

An unusual case of "vegetable foreign body encapsulated in a vocal cord" is reported by R S Rosedale and H E Bozer 2 The foreign body resulted in periodic attacks of hoarseness over a period of three years, becoming progressively worse with time Of particular note is not so much the fact that a polyp was removed from the vocal cord as that this represents the first case recorded in which such a growth contained within it a grain of wheat Of greater interest, rather, is the significance, so well stated by Rosedale and Bozer, of a chance inclusion of the grain of wheat in the sectioning of the polyp for microscopic study This foreign body occupied such a small area of the polyp which it undoubtedly produced that it might otherwise have been overlooked, except in a serial study of the specimen

Paralysis

Treatment — An unusually straightforward analysis of the problems attending the treatment of bilateral ("abductor") recurrent laryngeal nerve paralysis is given by W. Stevenson.³ Various phases relating to the treatment of such types of paralysis of the larynx have been presented in many of the preceding volumes. A concise summary is, nevertheless, not amiss here.

Bilateral paralysis, which most commonly is due to a peripheral injury of both recurrent larvngeal nerves following thyroidectomy, either by direct trauma or by scar tissue exerting traction, is a serious and alarming complication The great danger is that of acute asphyxiation at any time due to the closure of the glottis by the "paralyzed" vocal cords becoming fixed just a millimeter or two lateral to the midline of the laryngeal lumen (glottis); subsequently, any minor event, inflammatory or emotional, brings the cords, true and false, tightly together and death follows unless someone is present to open the trachea

Classically, in these states, a period of hoarseness or aphonia is followed by an improvement or return of the voice as the paralytic vocal cords tend to become spastically adducted This sequence is a sign of great danger rather than of improvement, impending asphyxial states are readily prognosticated at this time by a simple examination of the larynx Indirect laryngoscopy discloses a midline (paramedian) fixation of the vocal cords Yet, many surgeons consider the return of phonation as a good prognostic sign As Stevenson so well points out, these cases disprove rather than support Semon's hypothesis relating to vocal cord "shifts" in various forms of paralysis of the larvnx

The ideal treatment would be that of end to end suture of the injured nerves or anastomosis with other functioning nerves, thus restoring physiologically the action of the paralyzed muscles. Of significance is Stevenson's observation



Fig 1—Photomicrograph of fungus illustrating character of hyphae and blastopores (×500), (Courtesy Annals of Otol, Rhinol and Laryngol, Dec, 1936)

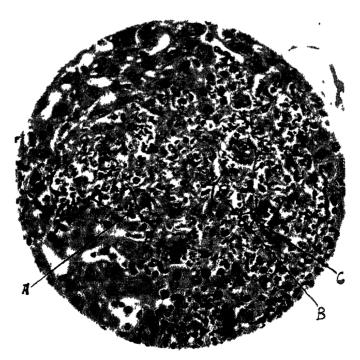


Fig 2—Photomicrograph of liver of rabbit following inoculation with a pure culture of the organisms isolated from the patient's larynx ($\times 900$) (Courtesy Annals of Otol, Rhinol and Laryngol, Dec, 1936)

that according to Semon's "law," section of the recurrent nerves should place the cord in the cadaveric* position with good airway, relieving the dangers of suffocation, though with much damage to the voice; "practically, such a procedure has never been successful" The lack of effectiveness from such methods is due to the fact that these abnormal states already have their genesis in a complete recurrent laryngeal nerve destruction, and a secondary hyperactivity of muscles being the effect of intact nerve pathways other than the above. Such hyperactivity resulting in fixation of the vocal cords in the midline is attributable to psychoneurotic as well as to organic factors

Until more information is available. there are but two forms of temporizing treatment available One is purely prophylactic, and concerns only the provision of an adequate air passage by means of an orderly tracheotomy The other is directed at a restoration of the patency of the laryngeal lumen, with as little destruction of the phonatory structures as possible, by plastic procedures on the vocal cords, arytenoids or upon both Stevenson advocates Hoover's method of submucous cordectomy (cordopexy procedures have been described in the 1934 and 1935 service volumes), as modified by Lore who recommends total ablation of the arytenoid cartilages The end result was an ample airway and a voice of fair strength and quality

Herpes Zoster

Bullous eruptions of the mucosa anywhere represent lesions analogous to dermatologic diseases. Herpes zoster of the epiglottis is to be differentiated from

other dermatord lesions of the mucous membranes as herpes simplex, pemphigus, aphthous stomatitis, papular eruptions of syphilis, gummata and tuberculosis according to Y Franchini. Treatment is mainly systemic and the relief of pain locally by the use of such anesthetic preparations as orthoform and procaine hydrochloride. Franchini advo-



Fig 3—Drawing shows a mirror view of the larynx. The infiltrated vocal cords and interarytenoid tissues presented a nodular appearance and were covered with a thin grayish exudate and an occasional whitish elevation (Courtesy Annals of Otol, Rhinol and Laryngol, Dec., 1936)

cates also the use of intravenous injections of urotropine, autohemotherapy and injections of sodium hyposulfate

Infections

The tendency has been to group acute infections of the larynx which extend into the bronchi and bronchioles under the heading of "Sporadic or Endemic Acute Laryngotracheobronchitis", such nonspecific infections are now considered as clinical entities. The etiology, symptoms and treatment are to be found outlined in detail in the preceding volume. Of importance this year is the effect of sulfanilamide upon these acute processes, particularly because of the predominance of the streptococcus in acute laryngo-

^{*&}quot;Cadaveric" denotes complete denervation of a vocal cord, either in high vagus nerve or combined superior and recurrent laryngeal nerve destructions



Fig 4—Photomicrograph of fungus classified as belonging to genus Candida from culture on potato water (×500) (Courtesy Annals of Otol, Rhinol and Laryngol, Dec, 1936)



Fig 5—Photomicrograph of edge of colony on a slant of glucose agar illustrating branching and irregularly spaced verticils The black masses consist of yeast-like cells (×80) (Courtesy Annals of Otol, Rhinol and Laryngol, Dec, 1936)

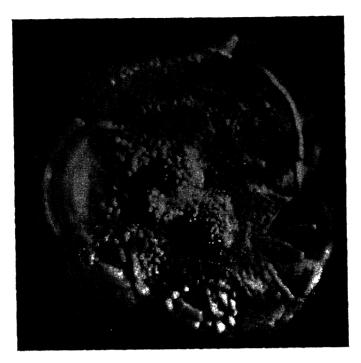


Fig 6—Photograph of giant colony after 40 days of growth (Courtesy Annals of Otol, Rhinol and Laryngol, Dec, 1936)

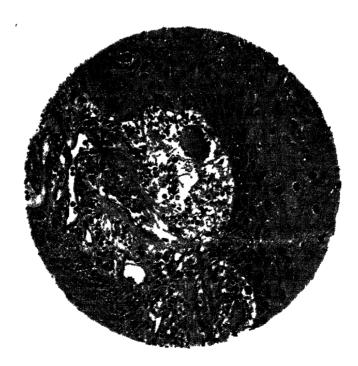


Fig 7—Photomicrograph of tissue from the patient's larynx, illustrating the granulomatous character of the lesion $(\times 400)$ (Courtesy Annals of Otol, Rhinol and Laryngol, Dec, 1936)

tracheobronchitis and the potency of sulfanilamide against certain strains of streptococci M P Spearman and W E Vandevere⁵ add little in their report to the foregoing, but in an appended communication, they remark that two cases have recovered in which the drug sulfanilamide was given. Since organisms other than the streptococcus are found in this type of process, early



Fig 8—Drawing of mirror image of laryn. The changes are more marked on the left vocal cord and in the interarytoid area which present a nodular appearance. The right vocal cord is swollen and presents a wrinkled appearance (Courtesy Annals of Otol, Rhinol and Laryngol, Dec, 1936)

diagnosis followed by tracheotomy, suction, humidification of the air and supportive measures including blood transfusion are considerations of highest import, convalescent scarlet fever sera and the like, diphtheria antitoxin and drugs such as sulfanilamide are yet to be employed judiciously and only as adjuncts

Yeast-like fungus infections of the larynx primarily, according to the literature review by L A Clerf and C J Bucher⁶ have been so diagnosed in only six cases. These writers report three proved and two suspected cases of fungus involvement at this level of the respiratory tract. Three manifested signs

and symptoms of a tuberculous process, but repeated pulmonary and cystologic examinations failed to reveal any tuberculous factors. Fungi were demonstrable in all of the chronic ulcerative and granulomatous lesions of the larynx. The characteristics of these parasites were studied in detail, including cultivation on a series of media and their chemical reactions and autopsy studies of rabbits following their inoculation.

The taxonomy of these organisms is controversial Treatment is apparently lacking in effectiveness Potassium iodide in increasing doses perorally, sodium iodide intravenously in 30-grain doses, tartar emetic (one per cent solution) intravenously in ascending doses were used with little marked improvement One patient received inhalations of ethyl iodide with definite improvement, but symptoms of ataxic paraplegia developed, its discontinuance was followed by recovery from the paraplegia Roentgen irradiation only slightly improved one patient Of significance is the tendency for recurrence and the persistence of the organism in the majority of the cases reported The prognosis is obviously a guarded one Though these fungi do not appear to be fatal per se, scarring and stenosis of the larvnx are sequalae, since they usually persist in the larynx. exacerbations are evidently the rule

Tuberculous infections of the larynx have not received the attention in the literature this year as in other years J B Greene⁷ reports a few cases which indicate that a high sedimentation curve (Cutler's chart) indicate a favorable and a low, an unfavorable prognosis, particularly when studied following a simple cauterization of such local tuberculous processes as are to be found within the larynx

Helium Gas in Respiratory Tract Disease—A valuable adjunct has been

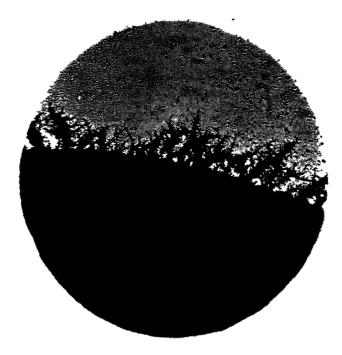


Fig 9—Photomicrograph of margin of colony on glucose agar, illustrating dendroid clusters of the organism (×80) (Courtesy Annals of Otol, Rhinol and Laryngol, Dec, 1936)

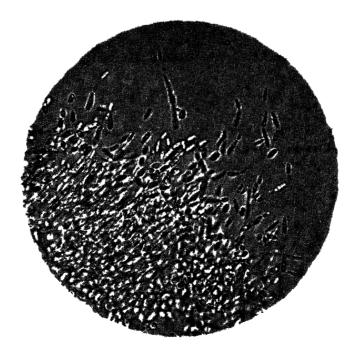


Fig 10—Photomicrograph of margin of a colony on beerwort agar, illustrating hyphae and elongate lacrimiform blastopoies in parallel arrangement (×80) (Courtesy Annals of Otol, Rhinol and Laryngol, Dec., 1936)

introduced by J D Kernan and A. L Barach⁸ in the palliative treatment of obstructive lesions of the lower respiratory tract Because of the molecular lightness of helium, a mixture of 80 per cent helium and 20 per cent oxygen is three times lighter than similar ratios respectively of nitrogen mixed with oxygen The effects of the administration of such gases,—particularly under a

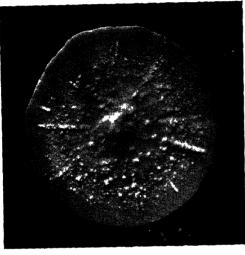


Fig 11—Photograph of giant colony of fungus after 40 days (Courtesy Annals of Otol Rhinol and Larvingol, Dec., 1936)

head tent which permits the additional benefit of maintaining a positive pressure of 1 to 3 cm (of water) of the respired mixture,—are a lightening of the respiratory burden of the patient and consequently a relative increase in the patient's defensive powers Kernan and Barach found that the use of such gases tided their patients, particularly infants, over such acute respiratory infections as laryngotracheobronchitis, laryngeal croup, laryngeal edema and bronchopneumonia Tracheotomy must still be the method of choice in providing adequate space for the passage of air, either by virtue of its being placed below an obstructive lesion of the larynx, or of its assistance from above in the aspira-

tion of tenacious secretions from the tracheobronchial tree

Technic-A helmet hood type of apparatus which makes closure at the neck possible is preferable to a body enclosing tent, even for infants and children This permits the helium-oxygen mixture to be administered to the patient under positive pressure. The oxygen and helium are supplied from one common tank, and a second oxygen tank used to modify the concentration Otherwise, the concentration of oxygen within the helmet must be determined constantly in order that asphyxia from excessive amounts of helium be avoided accident is greatly obviated by the use of a common helium-oxygen tank as mentioned The concentration of helium is varied from 78 to 65 per cent depending on the degree of anoxemia and respiratory distress

Carcinoma

Although this subject has been thoroughly discussed in the previous years, a report by H E Martin,9 representing the Memorial Hospital of New York, warrants additional comment on the The concepts and matter this year attitudes, more or less, of the general surgeon are expressed by Martin-at some variance with those of the experienced laryngologist-when he advocates a laryngotomy for inspection of the subglottic region in clinically suspected early cases of cancer of this region He reserves partial resections of the larynx for cases of intrinsic carcinoma, all other more advanced cases are managed by roentgen irradiation and radon seed implantations. The general surgeon's usual reasons against laryngectomy are given, namely, the magnitude of the operation (which is nonexistent in the hands of thoroughly trained laryngeal surgeons) and the loss of the voice (which too is of little significance considering the nature of the disease and the compensation for such a loss by the adequate voices obtained with the new artificial larynx—described in the volume of 1937).

Martin states that in the partial laryngectomy procedure which he employs for intrinsic cancer of the larynx, he removes the thyroid plate on the side involved since "the soft tissues overlying the cartilage..." form a thin layer anteriorly, so that the cartilage is very apt to be invaded, and its removal is a safethe laryngostomy opening A tracheotomy tube is placed in the lower angle, above which a cotton tampon prevents blood from entering the trachea Enough radon seeds are then implanted in the tumor mass to deliver a tissue dose of 10 SED (skin erythema doses) to all parts of the diseased areas A special laryngostomy tube is employed to maintain the opening throughout the period of treatment and observation Check-up examinations by stereo x-rays are made at 48 to 72 hour intervals for the first

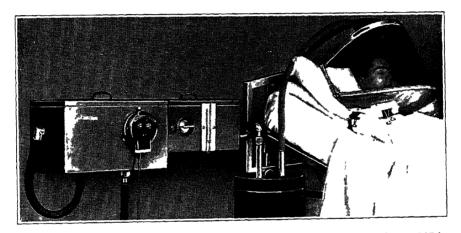


Fig 12-Helium and oxygen hood tent (Courtesy Arch Otolaryng, Oct, 1937)

guard against recurrences "in the attempt to retain function, no concession should be made to adequate excision of the disease" Such sound reasonings regarding proper surgical treatment are contradictory when Martin continues by detailing his procedure of partial resections even for anterior commissure tumors which invade or appear to invade both sides

Laryngostomy and implantation of radon seeds are resorted to in cases of "far advanced intrinsic" (origin intrinsic and secondary extrinsic characteristics by invasion) cancers. Local anesthesia is used, the cricoid and upper three or four tracheal cartilages are included in

week to confirm the proper placement and retention of the seeds. These are replaced if extruded. Reaction to the radium is first noticeable in about 10 to 12 days, when definite signs of regression, accompanied by an active congestion of the parts and the gradual development of a mucositis, appear. The height of this reaction takes place in about 25 to 30 days. Radionecrosis of cartilage may occur at this time with sequestration and extrusion of such portions.

The special laryngostomy tube is removed after six to eight weeks and the tracheotomy tube after a year or more, when the defect is closed by any of the plastic procedures. If the lumen of the

glottis is so contracted as to be inadequate as an air-conduit, the tracheotomy tube is left in place

The method of protracted fractional roentgenray irradiation of extrinsic types of cancer of the larynx as developed by Henri Coutard is advocated in its entirety by Martin as well as by the modern laryngologist. Details of this technic are to be found in this article

Acute radiation effects locally, both in the skin and mucous membranes, are desirably those of acute blistering. This state is best treated by external dressings of vaselinated gauze or hygroscopic ointments such as:

| Ŗ | Lanolin | 2 | |
|---|---------------------|---|---|
| | Zinc oxide ointment | 1 | |
| | Starch . | 1 | |
| | Liq petrolatum | q | S |

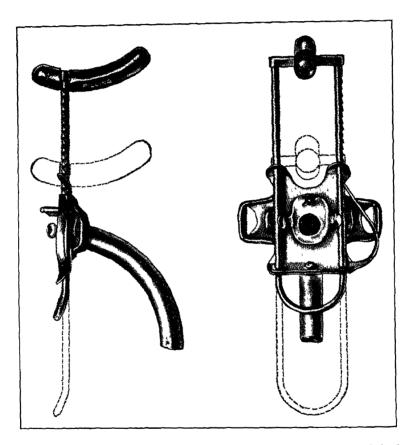


Fig 13 (Martin)—Special laryngostomy tube for maintaining the patency of the laryngostomy opening after implantation of radon seeds (Courtesy, Transactions American Academy of Ophthalmology and Otolaryngology, 1936)

Treatment of Complications and Sequelae of Radiation—General systemic reactions of chronic radiation sickness are manifested by listlessness, weakness and loss of weight with cachexia. The treatment consists essentially of reducing the areas of skin portals exposed to radiation.

Mucositis is treated only by relieving discomfort arising from the accumulation of viscid secretions *Irrigations* with saline solution and *suction* are adequate measures

Dysphagia is always present more or less. It must be ever relieved to maintain the nutrition of the patient. Nasal feed-

ing or even gastrostomy are to be employed until the patient is able to obtain sufficient nourishment by his own efforts.

Dyspnea is to be anticipated and laryngogenic asphyxiation due to swelling reactions are prevented by tracheotomy performed early rather than late

Pulmonary complications in the form of bronchopneumonia or pulmonary abscess are not uncommon, usually being the result of aspiration

Radionecrosis is a serious complication. When it does occur, no markedly successful measure is at hand to prevent a progressive course of destruction, sepsis and hemorrhage Treatment is limited to the well known patterns of surgical principles

Hemorrhage may occur as the result of erosion of one of the larger arterial branches by the disease itself or by radionecrosis and slough Tamponage is not often possible in the hypopharynx Ligation of the external carotid and particularly its superior thyroid branch is indicated

Xerostoma, or dryness of the mouth and pharynx, is due to a dysfunction, not only of the major salivary glands but also of the minor salivary glands in the mucosa of the palate, base of tongue and pharyngeal walls. It may be prevented by using small portals (50 to 75 sq cm) whenever possible. No active measure for its relief exists. It is temporarily relieved by frequent applications of liquid petrolatum or the chewing of gum. The secretions tend to return after a year or two

Artificial Larynx — The artificial larynx is advocated particularly because it demands so little from the patient as an adequate and simple means of restoring his social and economic status R H. Stetson¹⁰ prefers his patients to be subjected to a course of instruction in the swallowing and belching of air to pro-

duce the explosions essential to the production of esophageal speech. Stetson's objections to the artificial larynx are its monotonous tone; its harnessing of an instrument to a patient, pre-empting the use of one hand; and its unsightly and unpleasant aspects to women. In its place, he offers courses of study in the production of guttural esophageal explosions. These courses require the services of a well trained personnel and usually a considerable expenditure of time and effort, to say nothing of the cost, by the patient.

It is this editor's opinion that the latter program must eventually become a medical curiosity and source of interest only to the academician and pedagogue; the artificial larynx is the most economical and least taxing form of providing these patients with speech. Certainly, neither the former nor latter substitutes for normal speech mechanisms can be considered as esthetic by the widest stretch of imagination, the choice is rather between laryngeal malignancy with its relentless progress and laryngectomy with a simple means (artificial larynx) of voice rehabilitation

Tuberculosis of the Trachea

With the general increase in direct examinations of the respiratory tractas well as an increase of bronchoscopies in pulmonary tuberculosis—an enlightening has been attained in the concepts of not only tuberculosis of the lung proper, but also of its secondary manifestations at higher levels. It is known that tracheal and bronchial tuberculosis occurs as the result of an extension from a tuberculous peritracheal or peribronchial lymphadenitis. But not as well known is another source from within, which gives rise to a specific mucosal or submucosal infection To such types, P C Samson¹¹ applies the particular term of "tuberculous tracheobronchitis" This is in contradistinction to the former group, which he classifies as "tracheobronchial tuberculosis." The symptoms are mainly those of moderate to severe reductions in the size of the lumen in some portion of the airway, particularly in the bronchi and bronchioles The most constant symptom is wheezing or rattling, either inspiratory, expiratory, or both Paroxysms of coughing attend an obstruction to the passage of sputum. Massive obstructive atelectasis will develop if a lobar bronchus becomes completely blocked. Finally, persistence or increase in the productiveness of sputum and presence of bacıllı have been traced by Samson to bronchial or tracheal ulceration rather than to an activity within the parenchyma of the lung Bronchoscopic examination of such lesions discloses a number of pathologic types and phases as described in previous volumes under the heading of laryngeal tuberculosis Briefly, these changes within the mucosa vary from moderate hyperenna, infiltration and ulceration to granulomatous or tuberculomatous formations Healing is by scar tissue, which can cause moderate to complete cicatricial stenosis of a lumen

The diagnosis is obviously enhanced by direct, bronchoscopic examinations in addition to careful physical and roentgenologic surveys Upper lobe as well as peripheral obstructive lesions are best visualized by instilling opaque oils prior to roentgenography. The treatment is that of the general and pulmonary infection Local measures consist in the use of silver nitrate solutions and the cautery; removal of granulomas or tuberculomas. Roentgenray radiation is advised to help in the absorption of scar tissue. Care is to be exercised in the use of caustics, as they may in themselves produce cicatricial stenosis of a bronchial

lumen. J D. Kernan¹² advocates the direct application of ultraviolent rays with quartz rods.

The prognosis in ulcerative lesions. according to Samson (loc. cit.) is generally poor, "whether the patient was treated by bed rest only or by collapse therapy, and whether the designated treatment was instituted before or after the appearance of symptoms of tracheobronchial disease" Nonulcerative and nonstenotic lesions represent less active forms of tuberculous processes, and indicate somewhat better prognoses. In a differential diagnosis the following are to be excluded Nonspecific inflammations and ulcers, erosion of lymphatic nodes. neoplasms, syphilis, scleroma, asthma and extrabronchial conditions which may cause various degrees of tracheal or bronchial obstruction (compression stenoses)

NECK AND MEDIASTINUM

Infections of the Neck

Considering the many portals of infection to the deep structures of the neck and the ease with which infections "should" extend along the cervical fascial sheaths, it is surprising that there is not the expected frequency nor high degree of morbidity L C. Boemer¹³ reports a series of 75 cases seen during a threeyear period, 1934 to 1936 inclusively The purpose of his investigation was to determine wherein lay the greatest hazard to life Actually, it is to be expected that this lies in the involvement of the large blood vessels of the head and neck and in the extension into the mediastinum, Boemer found that the former represented the greatest hazard in his series of two deaths

The following table lists the origin and termination in this series

TABLE I TWENTY-SIX IN ADULTS

9 from lower third molar tooth

7 from cervical glands

3 from tonsil (one death, autopsy)

2 from mastoid (one death, autopsy)

5 from miscellaneous sources
Fracture of mandible
Ten days after tonsillectomy
Carcinoma of nasopharynx
Carcinoma of larynx

Source unknown
FORTY-NINE IN CHILDREN

38 from retropharyngeal lymph glands

11 from deep cervical glands

It should be noted that suppuration of retropharyngeal and deep cervical lymph nodes accounted for the condition in 49 cases in children, all recovered. Of the total number of 75 cases, only two deaths occurred — an unusually small number

The treatment is early surgical evacuation of the deeply situated abscess by opening from without the anterior (prestyloid) or posterior (poststyloid) compartments of the parapharyngeal space (pharyngomaxillary fossa) as the case may indicate by its genesis.

Mediastinitis

When the foregoing types of infections descend into the mediastinum, they form either a localized abscess or a diffuse cellulitis, termed "mediastinal abscess" and "phlegmonous mediastinitis," respectively, by H Neuhof 14 He found that the abscesses followed nontraumatic lesions, that both types occurred in cases of perforations of the esophagus and that phlegmonous mediastinitis resulted from acute nasopharyngeal infection. The latter genesis also produced a type of nonsuppurative mediastinitis which he assumed to be due to a lymphadenitis, subsiding spontaneously Another type, which Neuhof terms "incidental mediastinitis," occurs in septic states, or, in transit, in descending infection from the throat or ascending infection from the retroperitoneum. In six such cases, the lesion presented no clinical features and was a post-mortem disclosure.

Treatment—The treatment of mediastinitis should be first that of prophylaxis, according to Neuhof, in the prevention of cervical infections from descending into the neck and mediastinum by proper drainage higher up or by prophylactic mediastinotomy (See: Supplemental Volume, 1935), which A. C. Furstenberg and L. Yglesias¹⁵ call a "Heroic measure" In cases of esophageal perforations, this measure is a debatable procedure, but Furstenberg and Yglesias say, "one which definitely possesses life-saving possibilities."

Cervical mediastinotomy is best performed on the right side, for the anatomic reasons that the right compartment of the posterior mediastinal space is larger than the left, also the right contains more lymph nodes and is therefore the site of predilection for many inflammatory processes in this region traumatic cases, the incision is on the side of the lesion Using local anesthesia, an incision from 2 to $2\frac{1}{2}$ inches (5 to 6 cm) long is made over the anterior margin of the sternocleidomastoid muscle down to the supraclavicular notch When the sternocleidomastoid, sternohyoid and sternothyroid muscles have been exposed, these structures, together with the contents of the carotid sheath, are retracted laterally, exposing the trachea and, at a deeper level, the right side of the esophagus It may be necessary to elevate the right lobe of the thyroid, in which event care must be taken not to injure the inferior thyroid artery, which enters the gland on its posterior surface close to its inferior pole At this point one must choose to enter by blunt dissection either the anterior mediastinum, which lies between the trachea behind and the arch of the aorta in front, or the posterior mediastinum along the lateral wall of the esophagus A guide to the procedure of choice might be found in a study of the etiologic factors producing the abscess A drainage tube is inserted and suction is applied at frequent intervals advantage may be derived from postural drainage by placing the patient in the Trendelenburg position When the infection of the mediastinum is below the fourth dorsal vertebra, posterior drainage is considered to be the method of choice by the thoracic surgeon An exception is made by Furstenberg and Yglesias to this general rule in the case of mediastinitis arising from cervical infections, stating "To drain an abscess through the tissues which it has invaded is, we believe, a surgical axiom which in no other region of the body can be more advantageously applied"

Tumors of the Neck

A. E Hertzler¹⁶ reports opportunely on the waywardness in the present trends to treat many diseases by "machines" rather than by more orthodox surgical methods Calling attention to the difficulty in establishing a bonafide diagnosis in cases of new growths of the cervical regions, Hertzler does well to call forth the value of the surgical approach for the important reason of obtaining adequate tissue for at least microscopic study if not as a means for obtaining a cure As a point further in the value of surgery, even in inoperable or radiosensitive tumors, he mentions the assistance to the patient in removing surgically a mass of tissue, to be followed by irradiation, in that such an excision reduces the demands upon the organism to absorb and eliminate its tumorous masses In addition, a surgical dissection of cervical lymph nodes produces less bodily discom-

fort than does x-ray treatment Finally, considering the ultimate fate of these patients, a definite consideration to the patient exists in choosing palliative methods that are the least incapacitating. In this respect, adequate irradiation, according to Hertzler, is definitely a more severe form of palliative treatment than a block dissection of the neck

The foregoing statements are not at all irrational when the facts regarding these tumors as known today are reviewed As so well established, malignant new growths are either radioresistant or radiosensitive. In the former group, within the neck, there are the branchiogenic (gill cleft) cysts and malignancies, neurogenic tumors, lymphangiomas, hemangiomas, and carotid body tumors, in the latter, Hodgkin's disease, lymphosarcomas and lymphoepitheliomas Although each special type has certain specific features clinically, these are not always well marked either early or late in the course of its growth Incision for biopsy should therefore precede any and every course of radiotherapy And notwithstanding a selection of the latter forms of therapy, excision of the mass is rational, followed, of course, by irradiation after the wound has healed

To sum up the results of (a) surgery, (b) irradiation and (c) a combination of the two, Hertzler was surprised to discover from his extensive experience that malignant growths as (1) Hodgkin's disease reacted in a fatal manner in the same length of time whether treated by x-ray or by surgery A combination of two did result in a prolongation of life over that obtained by either method alone (2) Lymphosarcoma extends notably toward the mediastinum by way of the lymphatics Such tumors have been found to react similarly to Hodgkin's disease (3) Lymphoepi-

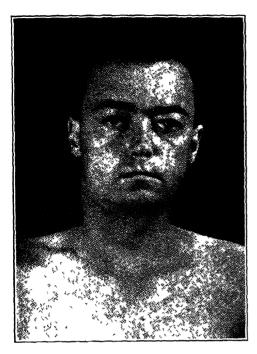


Fig 14—Hodgkin's disease A single ovoid tumor, movable on palpation No other enlarged glands discovered at operation (Courtesy, Southern Surgeon, Feb., 1937)



Fig 16—Hodgkin's disease Distant glands involved Marked anemia (Courtesy, Southern Surgeon, Feb., 1937)



Fig 15—Hodgkin's disease Ovoid on inspection, multilobular on palpation and at operation (Courtesy, Southern Surgeon, Feb, 1937)



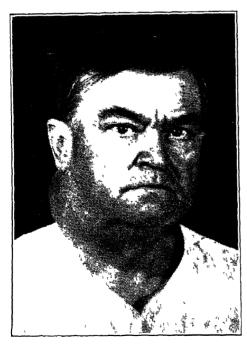
Fig 17—Lymphosarcoma Bosselated but solitary tumor, skin unchanged, elastic, even semifluctuant (Courtesy, Southern Surgeon, Feb , 1937)



 F_{1g} 18—Lymphosarcoma Many incisions had been made under the impression that suppuration was present (Courtesy, Southern Surgeon, Feb , 1937)



Fig 20—Lymphoepithelioma the size of a hickory nut occupying the typical position below and behind the angle of the jaw (Courtesy, Southern Surgeon, Feb, 1937)



 $\begin{array}{cccc} F_{1g} & 19 \\ \hline Lymphoepithelioma & of medium \\ grade & The tumor was ovoid, slightly bosselated, firm but elastic (Courtesy, Southern Surgeon, Feb., 1937) \end{array}$



Fig 21—Neuroblastoma forming a firm, slightly ovoid tumor in the midposition of the neck below and behind the sternomastoid muscle (Courtesy, Southern Surgeon, Feb, 1937)



 F_{1g} 22 — Lymphangioma occupying the supraclavicular fossa The skin is unchanged, the mass very soft on palpation (Courtesy, Southern Surgeon, Feb , 1937)



Fig 24—Lymphangioma of the submaxillary region Radiation produced in a few days a hard painful mass (Courtesy, Southern Surgeon, Feb , 1937)



Fig 23—Hemangioma of the supraclavicular fossa The bluish tumor is apparent through the skin (Courtesy, Southern Surgeon, Feb., 1937)



Fig 25—Gill cleft cyst Ovoid soft elastic tumor palpable in the floor of the mouth when pressed on externally (Courtesy, Southern Surgeon, Feb., 1937)

theliomas, though usually radiosensitive, have in some of Hertzler's cases been radioresistant Recurrences were prompt no matter what the treatment. (4) Neurogenic tumors fail to recur for long periods when removed early. Late operation is hazardous and futile.

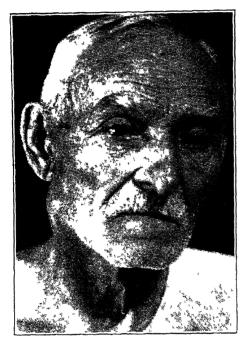


Fig 26—Carcinoma of a gill cleft The tumor was hard, nodulated and but slightly movable No recurrence after radical operation followed by x-rays (Courtesy, Southern Surgeon, Feb, 1937)

Nonmalignant swellings as (1) angiomas may be destroyed or augmented by irradiation, in the latter event, an intense reaction results Radiation is not the treatment of election (2) Gill cleft cysts are obviously best removed surgically Radiation prior to biopsy and diagnosis confuses clinical differentia-(3) Thyroglossal and dermoid cysts end with their proper excision When subject to radiation the latter reacts promptly with intense inflammation in the wall of the cyst and adjacent tissue This type of reaction clinically excludes sarcoma (4) Carotid body tumors occur rarely, and are benign if removed early.

Hertzler's conclusions are:

- 1. "Surgeons have been too ready to send neck tumors, not definitely diagnosed, to the radiologist
- 2 "Operation secures tissue which makes diagnosis possible
- 3. "Radical operation alone on the average secures relief for as great a length of time as radiation alone The two together may secure better results
- 4 "Radical operation causes the patient no greater inconvenience than the absorption of the tumor after radiation
- 5. "The sum total of our knowledge is enhanced by the study of the tissue removed"

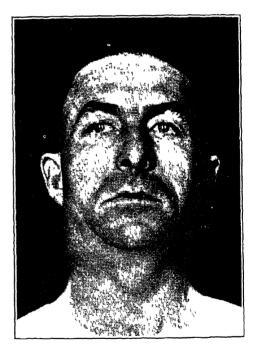


Fig 27-Carotid tumor A round nodule the size of a walnut occupied the crotch of the carotid bifurcation No recurrence after 18 years (Courtesy, Southern Surgeon, Feb,

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CLINICAL PATHOLOGY

By Robert A. Kilduffe, A M, MD

THE MECHANISM AND PRESENT CONCEPTS OF ANEMIA

The application of modern hematological methods to the study of anemia has not only modified the concepts of its mechanism but has evolved a classifica-

that a cause of anemia may be present without a coincident anemia following, a decreased rate of production cannot equally be compensated for by a decreased rate of destruction

Decreased rate of erythrocyte formation arises from a deficiency of sub-

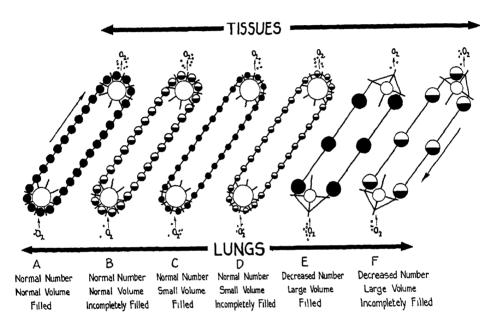


Fig 1—Schematic illustration of red cells functioning as units (cups) on an endless-chain conveyor A, Normal red cells B, Red cells of normal size partly filled with hemoglobin (normocytic, hypochromic anemia) C, Small red cells completely filled with hemoglobin (microcytic, hypochromic anemia) D, Small cells, partly filled with hemoglobin (microcytic, hypochromic anemia) E, Large cells, completely filled with hemoglobin (macrocytic, hyperchrome anemia) F, Large cells containing a normal amount of hemoglobin (macrocytic, normochromic anemia) (Courtes), Jour Lab and Clin Medicine, February, 1937)

tion of clinical as well as hematological significance

Briefly stated, it may be said that there are but two fundamental underlying factors concerned in the production of anemia. An increased rate of loss or destruction of red cells, or a decreased rate of blood formation.

While, however, an increased rate of loss or destruction may be compensated for by an increased rate of production so (884)

stances necessary for their construction or maturation (such as iron, copper, the antipernicious anemia principle, vitamin C, thyroxin, or the "secondary anemia principle" of Whipple). In the myelopthisic anemias the deficiency is in the bone marrow which is unable to produce the needed number of cells. In the hypoplastic or aplastic anemias there is a partial or complete failure of the marrow cells to divide

Removal of erythrocytes from the peripheral stream occurs at an increased rate as a result of external or internal hemorrhage, hemolysis, mechanical destruction (as in malaria), or as an evidence of excessive activity on the part of the normal blood destroying mechanism.

In the ultimate analysis, the clinical importance of anemia depends upon the fact that there is a reduction below norAs the problem of anemia concerns itself primarily with hemoglobin and its carrier, the red cell, it is obvious that in addition to thinking of the red cell as a cup in an endless conveyor, the total mass of circulating red cells must be thought of as a vessel containing hemoglobin which, as shown in Fig. 2 varies enormously in size in blood dyscrasias affecting the red cells.

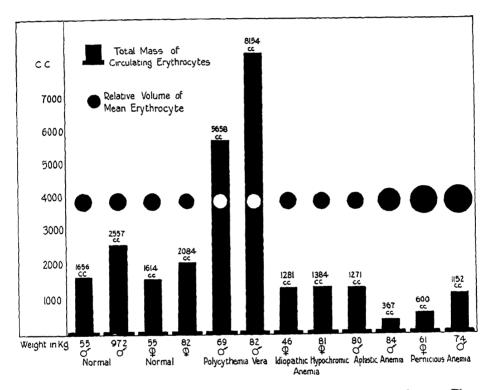


Fig 2—Variation in total mass of circulating red cells in various conditions. The circle indicates the relative volume of the unit of mass (the red cell) in each instance. (Courtesy, Jour Lab and Clin Medicine, February, 1937.)

mal in the capacity of the blood to transport the oxygen essential for animal life. The oxygen carrier of the blood is hemoglobin, the red cell, as Haden¹ points out, is merely a container and functions like a cup in an endless chain conveyor. So graphically and so clearly has Haden presented the modern concepts of anemia that his article will be freely drawn upon in this brief survey.

When a red cell is destroyed, hemoglobin is set free, iron is split off from the hemoglobin molecule, and bilirubin is formed as an end result of pigment metabolism

Therefore, in the absence of liver disease and biliary destruction, the degree of bilirubinemia furnishes an index of the rate of erythrocyte and hemoglobin destruction as indicated in Table 1

TABLE 1
RELATION OF BLOOD FORMATION AND DESTRUCTION TO BILIRUBIN AND RETICULOCYTE LEVEL

| Bilirubin | Reticulocyte Count | | | | | | |
|------------------------------|---|--|--|--|--|--|--|
| Content Icterus Index | Increased (over 1 5%) | Normal (0 5–1 5%) | Decreased (under 0 5%) | | | | |
| Increased (over 6 units) | Increased blood destruc- tion with active bone marrow | Increased destruction without good marrow response | Increased destruction with inactive bone mar- row or impaired de- livery of red cells | | | | |
| Normal (4–6 units) | Active bone marrow without excessive destruction | Decreased marrow without excessive destruc- tion of red cells | Decreased formation or impaired delivery of red cells without ex- cessive destruction | | | | |
| Decreased (under 4 units) | Decreased destruction of hemoglobin due to iron deficiency, active cell formation in mar- row | Decreased destruction of hemoglobin Decreased formation of hemoglobin, normal cell formation in marrow | Decreased destruction of hemoglobin Decreased formation of hemoglobin Decreased cell formation in marrow or impaired delivery of cells | | | | |

Other indicators of red cell activity are shown in Table 2, from which it is possible to calculate the balance between erythrocyte formation and destruction, the rate of regeneration, the lack of the erythrocyte maturing factor, and the deficiency of iron

The relation of blood findings to the rate of red cell destruction and formation is indicated in Table 3

From these factors anemias may be classified clinically as follows

Clinical Classification of Anemia—

- I Increased blood loss-
 - 1 Mechanical loss from hemorrhage
 - 2 Accelerated red cell destruction by
 - (a) Hemolytic agents
 - (b) Rapid red cell removal (as in congenital hemolytic icterus, overactivity of reticulo-endothelial system, or defect in cell structure)

II. Decreased blood formation-

1 Quantitative decrease in red marrow from aplasia

- 2 Quantitative depression of marrow activity
- 3 Qualitative decrease in marrow activity from deficiency of specific substances necessary for normal marrow activity
 - (a) Deficiency in supply, absorption or use of erythrocyte maturing factor
 - (b) Deficiency in supply, absorption or use of iron

It becomes obvious that careful and complete laboratory studies are essential for the clinical classification of anemias, as indicated in Fig. 3

It is, of course, apparent that recognition of the existence of anemia is only a preliminary before methods for its treatment and control can be planned. The next, and most important, step is to determine its nature and underlying mechanism in order that treatment may be planned, purposeful, and intelligent

It is equally apparent that a primary appreciation of the mechanism of the formation, circulation and destruction of the normal red cell. This cycle is illus-

TABLE 2
Measures of Red Cell Activity

| Factor | Indicator |
|---|--|
| Balance of red cell and hemoglobin formation and destruction Rate of destruction of red cells Rate of regeneration of red cells. Deficiency of iron Deficiency of erythrocyte maturing factor (EMF) | Red cell count and hemoglobin content Level of bile pigment in plasma Level of reticulocytes in circulation Hypochromia and microcytosis of red cells Macrocytosis of red cells |

TABLE 3

RELATION OF BLOOD FINDINGS TO RED CELL FORMATION AND DESTRUCTION

| RELATION OF BLOOD FINDINGS TO RED CELL FORMATION AND DESTROCTION | | | | | |
|--|--|--|--|--|--|
| Active bone marrow | [Increased number of reticulocytes, basophilia, nucleation Slight increase in mean erythrocyte volume if reticulocytosis is marked Often an increase in leukocytes and platelets unless destruction is more active than normal The number of cells is increased. | | | | |
| Inactive bone marrow | Decrease or absence of reticulocytes, basophilia and nucleation If blood destruction is normal or increased, the cell count decreases | | | | |
| Increased red cell and hemo- globin destruction | Increase in bilirubin content of plasma, decrease in number of cells unless compensated for by increased marrow activity. | | | | |
| Decreased hemoglobin de- | Decrease in pilirubin content of plasma. | | | | |
| Deficiency in erythrocyte maturing factor (pernicious anemia, | (Anemia with increase in mean erythrocyte volume (increased volume index) | | | | |
| Deficiency in iron (iron deficiency anemia, chronic hemorrhagic anemia) | Anemia with hypochromia of red cells (decreased color index), microcytosis (decreased volume index), if hypochromia continues | | | | |
| Hemolytic anemia | Anemia with increased icterus index, reticulocytosis if marrow responds to increased need | | | | |
| Anemia due to decrease in amount or activity of mar- row (aplastic or hypo- plastic anemia) | Anemia with cells of normal size and hemoglobin content, de- crease in reticulocytes | | | | |

trated so clearly in Fig 4 as to require no further description

As Haden has pointed out, the mechanism of anemias and the underlying fundamental fault responsible for their production can be shown in a diagram, those presented below being taken from his article

Fig 5 shows the mechanism of the anemia following acute hemorrhage

When blood loss is continued it is apparent from Fig 6 that the fundamental defect is in the supply of iron to the

marrow as a result of which the red cells are small (volume index 067) and have a decreased hemoglobin content (color index 04). The therapeutic indications are obviously to control blood loss and supply iron

The cycle of events in the case of a hemolytic anemia of toxic origin, such as may be seen following the use of such a drug as phenylhydrazine, for example, involves a compensatory hyperactivity of the bone marrow in an effort to balance the excessive red cell destruction. This

is indicated by reticulocytosis. The rapid removal of the damaged red cells from the circulation results in an increased output of iron and bile pigment and the icterus index is hence increased. As there is no lack of building materials,

spherocytic rather than biconcave discs As the abnormal cells have a greatly shortened life span they are rapidly removed from the circulation with a consequent increase in the output of bile pigment and iron There is thus a rapid

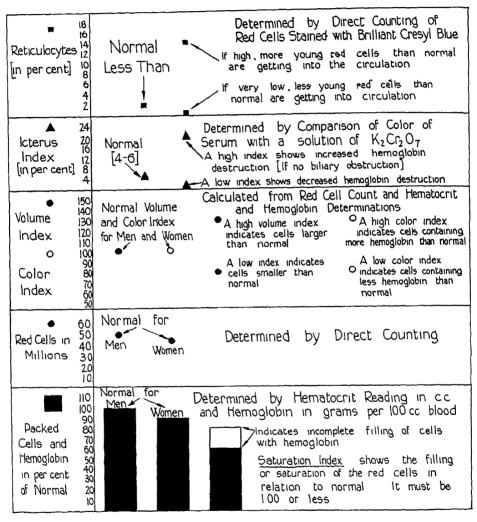


Fig 3—Study of blood and interpretation of findings in anemia (Courtesy, Jour Lab and Clin Medicine, February, 1937)

there is no therapeutic indication other than to remove the primary cause; that is, the toxic drug.

In congenital hemolytic icterus, there is also an ample supply of building materials, the fundamental factor in this disease being an anatomic defect in the shape of the red cells which are

flow of red cells from the marrow where they are produced to the spleen where they are filtered out. As the anatomic defect is therapeutically inaccessible, removal of the filter by *splenectomy* is the only remedy

A condition presenting several points of similarity is sicklemia in which there

is also a fundamental anatomic defect. Here, again, there is bone marrow hyperactivity (reticulosis) and increased red cell destruction (icterus index high), and again splenectomy is the treatment of choice. However, the results, while

form of anemia and for this no treatment is available.

Instead of a hemolytic anemia drug intoxication may produce an anemia consequent upon bone marrow aplasia, as after the prolonged use of arsenicals

NORMAL RED BLOOD CELL

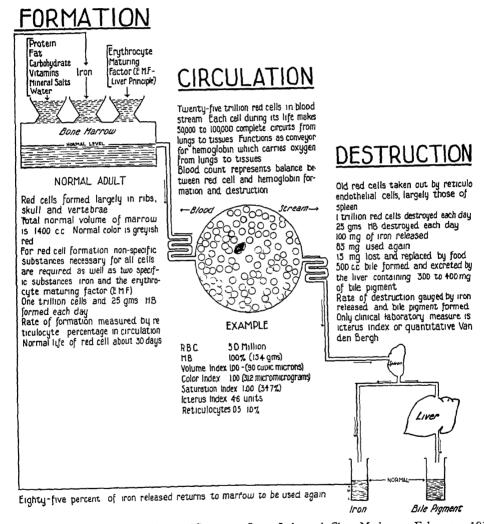


Fig 4-Normal red cell physiology (Courtesy, Jour Lab and Clin Medicine, February, 1937)

good are not as brilliant as in hemolytic jaundice because some degree of anemia remains after splenectomy, showing that the increased splenic activity is not the sole cause of the condition. There is reason to believe that increased red cell fragility is an important factor in this

in susceptible individuals. In this case, though there is an ample supply of building material the facilities for utilizing it are diminished and in this case treatment must be directed toward a restoration of the bone marrow to a normal functional activity

RED CELLS IN ANEMIA DUE TO ACUTE HEMORRHAGE

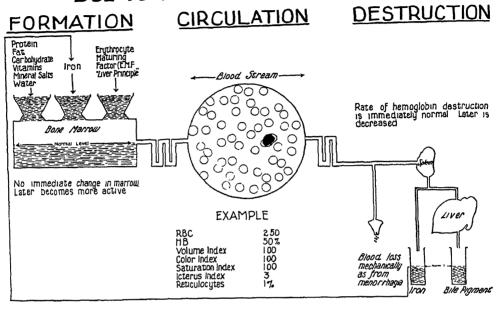


Fig 5—Physiology of red cells after an acute hemorrhage (Courtesy, Jour Lab and Clin Medicine, February, 1937)

RED CELLS IN ANEMIA DUE TO CHRONIC HEMORRHAGE

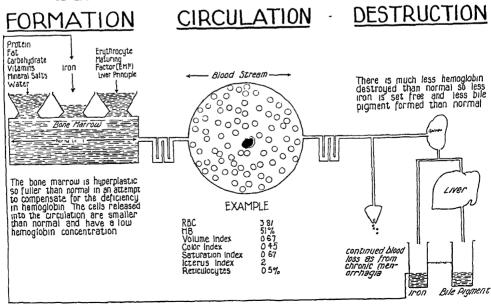


Fig 6—Physiology of red cells after a chronic hemorrhage (Courtesy, Jour Lab and Clin Medicine, February, 1937)

RED CELLS IN ANEMIA DUE TO QUANTITATIVE DEPRESSION OF MARROW ACTIVITY AS BY TOXEMIA FROM CHRONIC NEPHRITIS

FORMATION CIRCULATION DESTRUCTION Protein Pat Erythrocyte Moturing Factor (EMF) Carbohydrate Vitamins Mineral Salts Iron liver Blood Stream less calls and hemoglobin are destroyed so less iron is set free and less bile pigment formed than normal Water 0 0 0 Bone Marrow Ô 0 0 Here the marrow is normal in a-mount but does not function at the normal rate so fewer cells than normal are released into the circulation Live EXAMPLE 195 35% 0.92 0.92 100 RHB NB
Volume Index
Color Index
Saturation Index
Icterus Index
Reticulocytes 7

Fig 7—Physiology of red cells when the function of marrow is slowed up (Courtesy, Jour Lab and Clin Medicine, February, 1937)

RED CELLS IN ANEMIA DUE TO DEFICIENCY OF ERYTHROCYTE MATURING FACTOR-EMF.

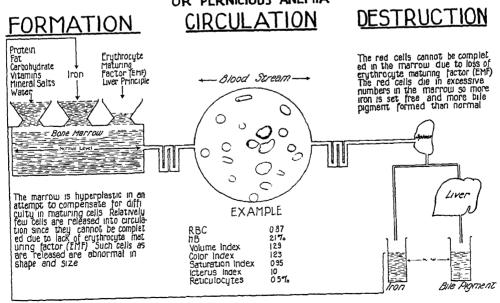


Fig 8—Physiology of red cells when building materials are deficient (pernicious anemia) (Courtesy, Jour Lab and Clin Medicine, February, 1937)

The anemia accompanying leukemia is also an expression of bone marrow depression resulting from the hyperplasia of myeloid tissue at the expense of erythrogenic tissue. The indication here is for a decrease in the amount of myeloid tissue (radiation) which, however, is palliative and temporary rather than curative

tion Such an anemia is illustrated by that seen in lead poisoning.

Here the hematopoietic mechanism is normal but does not operate at the normal speed

The most important advances in the treatment of anemias have been made in the types caused by lack of building material, so to speak

RED CELLS IN ANEMIA DUE TO DEFICIENT INTAKE OF IRON

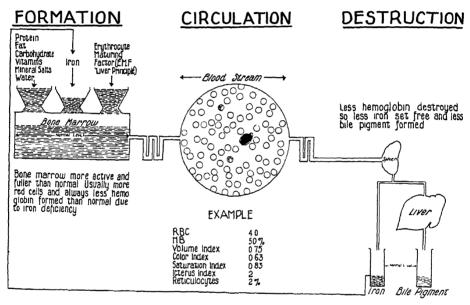


Fig 9—Physiology of red cells when building materials are deficient (iron deficiency anemia) (Courtesy, Jour Lab and Clin Medicine, February, 1937)

Toxemia may produce a quantitative depression of the bone marrow as shown in Fig. 7

Anemia may result from the inability of the bone marrow to utilize the erythrocyte maturing factor which may arise from a variety of factors. The treatment depends upon detecting the underlying cause producing the bone marrow inefficiency. Where anemia is dependent upon an inability to utilize the iron intake, not from an inadequate intake, the obvious treatment is to find and remove the obstacle to iron utiliza-

In Fig 8 is shown the mechanism of anemia dependent upon a defect in the supply to the marrow of the erythrocyte maturing factor

As the factor in question is furnished by the liver largely, the obvious therapeutic indication is to supply it by the administration of liver, liver concentrates, or gastric tissue

While the erythrocyte maturing factor is commonly spoken of as the antipernicious anemia factor, it is of practical importance to emphasize that the mechanism underlying the anemia of sprue and similar disorders producing macrocytic anemias is the same and the therapeutic indications also the same.

The mechanism of anemias arising from impaired assimilation or deficient intake or iron is apparant from Fig 9.

As the diagram indicates the treatment consists of an adequate supply of iron.

THE BONE MARROW AND BLOOD DYSCRASIAS

The bone marrow has long been recognized as an important center of hematopoiesis but only rather recently have simple methods for its study been developed.

Bone marrow biopsy was apparently first suggested and described by Ghedini in 1908 but only since Seyfarth,² Peabody,³ and particularly Arinkin,⁴ who has given us a simple technic for sternal puncture, has the method been applied with any frequency to the study of blood dyscrasias, especially those affecting the leukocytes

It is unnecessary here to describe the technic of bone marrow biopsy or to enter into the discussion between those who believe that specimens secured by trephine blocked and sectioned as a tissue are preferable to those secured by aspiration and examined in stained smears. The latter procedure is simpler and has been more widely used and most of the reports to be summarized have been thus secured.

It is, of course, obvious that in diseases of the blood the blood pictures depend, not only upon the phenomena attendant upon growth and destruction, but also upon the varied factors governing the maturation and release of blood cells from the hematopoietic centers. Bone marrow studies have clearly demonstrated that the existence, nature

and degree of such influences upon such hematopoietic centers as the bone marrow are, however, far from obvious from a study of the peripheral blood.

Thus, Dameshek⁵ has shown that in both pernicious anemia and primary hypochromic anemia, conditions in which the peripheral blood picture suggests bone marrow hypoplasia, the bone marrow may nevertheless be definitely hyperplastic, while Fitzhugh and Krumbhaar⁶ have demonstrated a "pyoid" bone marrow associated with marked leukopenia

It is recognized, of course, that the peripheral blood picture represents the end result of varied and often complex factors. But in view of the fact that identical pathologic processes may be accompanied by diversified blood pictures and, further, that identical blood pictures may be encountered in fundamentally different blood dyscrasias, the necessity for a study of what lies behind the blood picture becomes apparent

Dameshek (*loc cit*) from a study of both smears and sections in 200 necropsy specimens, presents the following as representing the approximate cellular constituents in normal (rib) marrow:

Ratio of nucleated erythrocytes to leukocytes approximately 1 1 (variation—from 0 6 to 12 to 1)

Differential count

Mature neutrophiles 2 - 5 per cent
Metamyelocytes 20 - 40 per cent
Myelocytes 30 - 50 per cent
Premyelocytes and myeloblasts 1 - 5 per cent
Eosinophiles 1 - 5 per cent
Histocytes 1 - 2 per cent

Differential erythrocyte count normoblasts 80 per cent, erythroblasts 20 per cent From two to ten megakaryocytes are encountered for every 300 leukocytes (07 to 33 per cent)

Osgood⁷ who has studied the bone marrow extensively, gives the following as representing the differential count of normal bone marrow smears:

| Cell | Aver- age per cent | Range per cent |
|--|--|---|
| Polymorphonuclear neutrophile Eosinophilic neutrophile Basophilic neutrophile Staff Cells, neutrophilic Staff Cells, eosinophilic Staff Cells, basophilic Metamyelocytes, neutrophilic Metamyelocytes, eosinophilic Myelocytes, neutrophilic Myelocytes, neutrophilic Promyelocytes I Promyelocytes II Myeloblasts Lymphocytes Monocytes Normoblasts Pronormoblasts Erythroblasts Megaloblasts Granulocyte-erythrocyte ratio | 13 3 0 45 0 1 24 1 0 8 0 06 7 4 0 64 0 86 1 48 0 44 10 6 2 06 5 7 1 5 | 7-25 0-1 0-0 2 15-35 0 2-0 6 0-1 1-10 0-2 0-1 0-5 0-5 0-2 4-16 0-5 2-10 2-15 0-0 2 2 1-9 1 |
| | | |

Among the blood dyscrasias in which the bone marrow cells have been reported upon are the following

Pernicious Anemia - Dameshek (loc cit) reports as characteristic findings in relapse hyperplastic marrow without fat and showing large numbers of promegaloblasts and megaloblasts, often present in "islands" and showing numerous mitotic figures With the institution of liver treatment the bone marrow to a great extent resumes its normal appearance Similar findings are reported by Osgood (loc cit) and Young and Osgood8 comment that in untreated pernicious anemia the most characteristic change is an increase in the number of megaloblasts, thus corroborating the findings of Peabody3 (seven cases), Arınkın4 (ten cases), Barta⁹ (22 cases), Tempka and Braun¹⁰ (30 cases), and Holmes and Braun 11

Secondary Hypochromic Anemia —Dameshek reports on three cases, in

two of which there was an associated hypernephroma, the bone marrow being hypoplastic; in the third, associated with chronic hemorrhage, the erythroblastic tissue was hyperplastic. In hypochromic microcytic anemia, Osgood reports a marked increase in the number of pronormoblasts and normoblasts

Primary Hypochromic Anemia—The bone marrow picture in this condition has been described by Kaznelson, Reimann and Weiner¹² and by Dameshek¹³ as hyperplastic and resembling the appearance seen in pernicious anemia with large numbers of erythroblasts and normoblasts, megaloblasts not being found.

Congenital Hemolytic Anemia—There are apparently but few reported bone marrow studies in this disease. In two cases Dameshek (loc cit) reports a ratio of erythrocytes to leukocytes of 04 to 1 with a marked relative increase of erythroblasts and, in one case, a definite increase in histocytes.

Aplastic Anemia—In severe cases Dameshek reports the marrow as converted almost entirely into fat with a ratio of erythrocytes to leukocytes of 0 075 to 1, and an almost complete absence of nucleated reds Similar findings are reported by Osgood

Myelosis—In this condition the bone marrow findings would appear to vary directly with the type of disease—acute or chronic. In the chronic type—leukemic or aleukemic—the leukocytes are markedly increased (ratio of red cells to leukocytes 0.05 to 1 to 0.7 to 1) with a marked increase of myeloblasts, myelocytes, however, being practically normal (Dameshek). A significant increase in the -blast or pro-stage is strongly suggestive of leukemia of the corresponding type of diagnostic when the increase is marked (Osgood)

Lymphatic Leukemia—In chronic cases there is a varying degree of bone marrow invasion by lymphocytes with, apparently, but little disturbance of normal cell growth

Monocytic Leukemia (Reticulosis)
—In the acute type there is an overwhelming proliferation of histiocytes
with a diminution of the reticulum, in
the chronic type there is an increase in reticulum associated with
the presence of numerous giant cells
(Dameshek)

Agranulocytosis — Darling, Parker and Jackson¹⁴ report the outstanding feature in the bone marrow as lack of maturation of the granular series and hyperplasia of the stem cells in acute cases In those of longer duration they noted hypoplasia of the myeloid tissue with coincident appearance of numerous lymphocytes and plasma cells Other observers report a complete absence of mature neutrophils, metamyelocytes, and myelocytes (Dameshek), marked proliferation of myeloblasts which, however, fail to mature, complete absence of segmented forms, and infiltration of lymphocytes and plasmocytes (Custer¹⁵), (Osgood)

Polycythemia Vera—In four cases fat cells are reported as decreased in the bone marrow, megakaryocytes conspicuously increased and, in general, there was a generalized prolifieration of all three bone marrow elements (erythroblasts, myeloblasts, and megakaryocytes) (Dameshek) (Osgood)

Idiopathic Thrombopenic Purpura—From a study of six cases, in four of which no bone marrow changes were found, Lawrence and Knutti¹⁶ conclude that there may be two types of this disease, one in which bone marrow changes are absent, and one characterized by a decrease in megakaryocytes as described in the few available

reports of bone marrow studies in this condition. Dameshek (loc. cit) reports no bone marrow changes in one case. There may be an increase in erythrocytes, pronormoblasts, and in the more immature cells of the granulocyte series according to Osgood (loc. cit.).

Infectious Mononucleosis (Glandular Fever)—In two cases Freeman¹⁷ reports the marrow spaces packed with immature and mature lymphocytes and suggests that glandular fever may be an abortive, benign form of acute lymphatic leukemia

Hodgkin's Disease — In six cases Dameshek (*loc cit*) reports hyperplasia of the leukopoietic elements of the bone marrow with a marked increase in the leukocyte-erythrocyte ratio Immature leukocytes and megakaryocytes were conspicuously increased in numbers

Banti's Disease — As Dameshek (loc cit) comments, many cases diagnosed as Banti's disease are really some other disease, usually chronic aleukemic myelosis. In one case, accepted as probably Banti's disease, he found an increase in the leukopoietic tissues of the bone marrow with an increase in myeloblasts and premyelocytes as a marked feature.

The bone marrow has been subjected to examination in isolated instances and in some cases in small series of varied conditions other than those above mentioned

Among these are the lipoid histiocytoses (Gaucher's disease), Niemann-Pick's disease, xanthomatosis (also called Hand-Schuller-Christian's disease) in which "foam cells" (large cells of the monocyte series with vacuolated cytoplasm) are encountered, and in neoplasms with metastasis, in which tumor cells may be seen

Kingery, Osgood, and Ilge¹⁸ report sternal marrow puncture as a diagnostic aid in leukemia cutis and as a possible aid in the differential diagnosis of the lymphoblastomas

The results of sternal marrow studies in infants and children is reported upon by Kato¹⁹ who describes the following as characteristic and differentiating the bone marrow in infancy and childhood from that of the adult

(1) Relatively high percentage of erythrogenic and lymphoid elements, (2) relatively low percentage of myeloid elements; giving a low myeloid-erythroid ratio of 1 2 as compared to 3 4 in the adult

While this subject may be regarded as still in the formative stage, enough has been done to indicate that future studies of blood dyscrasias may well be fortified by studies of bone marrow preparations in conjunction with peripheral blood studies, and that from such correlated observations the future understanding of many blood dyscrasias at present but little understood, and now regarded as of uncertain origin, may well develop

POST TRANSFUSION REACTIONS

Despite the safeguards now surrounding the selection of a donor, post transfusion reactions—usually of the delayed type—are occasionally encountered. Their etiology is obscure and still the subject of discussion for the relation of anomalous or irregular agglutinins to their occurrence has not yet been consistently demonstrated or generally accepted.

Bates²⁰ in reviewing the experience of a transfusion team from 1929 to 1936 comments that in analyzing the reac-

tions encountered they were distributed as follows

Type IV responsible for 39 per cent of reactions

Type II responsible for 34 per cent of reactions

Type III responsible for 12 per cent of reactions

Type I responsible for 7 per cent of reactions

He believes that among the factors producing reactions the time element is of importance as shown by the subjoined analysis of 50 cases without reactions and 50 cases in which they occurred

Cases showing reaction

Donor

Average time, 13 5 minutes Maximum time, 75 minutes Minimum time, 5 minutes

Recipient

Average time, 21.7 minutes Maximum time, 50 minutes Minimum time, 6 minutes

Cases without reaction

Donor

Average time, 94 minutes Maximum time, 40 minutes Minimum time, 2 minutes

Recipient

Average time, 42 5 minutes Maximum time, 270 minutes Minimum time, 9 minutes

It is noted that in the transfusions without reactions the donor's time was definitely shorter and the recipient's time nearly twice as long as in the group in which reactions were seen. While there is no clear evidence that a rapidly given transfusion adds to the frequency of the usual chill and fever reaction, it does tend to crowd the right heart and to that extent is to be avoided

In 71 transfusions with the Scannell whole blood method, reactions occurred in 36 per cent while in 451 citrate transfusions the incidence of reactions was 13 8 per cent

It is entirely probable that some at least of the reactions after whole blood transfusions are attributable to the difficulty of cleaning the apparatus used in these methods. Many of the reactions characterized by headache, nausea, vomiting and urticaria are expressions of protein sensitivity, in which connection the passive transfer of allergens ingested by the donor prior to transfusion must not be forgotten. Such an incident is reported by W. T. Vaughan and D. M. Pipes 21

Hemoptysis, dyspnea and cyanosis, usually coming on during the transfusion are most likely the manifestations of small multiple emboli. These are most often seen in elderly people. In the presence of bacteremia reactions are not uncommon

From his experience Bates offers the following theses, not as facts, but as representing convictions

- 1 The intravenous injection of sodium citrate plays no direct part in the production of reactions
- 2 Rapid transfusion does not increase the changes of reaction except in cases of impending circulatory embarrassment which should be protected by slow transfusion
- 3 A previous recent transfusion does not make a reaction to transfusion from a different donor more likely
- 4 Aside from not being aided by the transfusion, leukemia, agranulocytic angina, subacute bacterial endocarditis, and splenic anemia show a high incidence of reactions
- 5 Patients in extremis not due to shock or hemorrhage are not helped by

transfusion and moreover are liable to dangerous reactions.

Culbertson and Ratcliffe²² reporting a case in which, though the donor and recipient were the same type and the bloods compatible in laboratory tests, a severe reaction occurred, demonstrated the presence of an irregular agglutinin

They propose the following method as a test for such anomalous agglutinins

Method:

- 1. Place three drops of serum in a 14 mm test tube and add one drop of cell suspension (three drops of blood from a 20 gauge needle to 4 cc of normal saline containing 02 per cent sodium citrate)
- 2 Shake to mix and incubate five minutes at 98.6° F $(37^{\circ}$ C)
- 3. Centrifuge three minutes at high speed
- 4 Note any evidence of hemolysis and then resuspend the cells and examine with a hand lens for clumping
- 5 Pour the fluid on a slide and examine under the microscope for agglutination

This procedure is of value where intragroup agglutinins were too low in titer to be detected in routine compatibility tests

COMPLEMENT FIXATION TESTS

Vacuum Dried Complement

In the past many endeavors have been made to preserve complement serum for use in complement fixation tests, particularly for use in complement fixation (Wassermann) tests for *syphilis*

While it has been found possible to preserve complement serum for several weeks by the addition of sodium chloride, until recently no method was successful for preservation over longer periods Flosdorf and Mudd.²³ however, have

recently described a method for the preservation of serum and other biological substances which undoubtedly will lead to revolutionary changes in these fields

The procedure is essentially one of rapid freezing at a very low temperature coupled with rapid dehydration from the frozen state under high vacuum, the process being continuous and conducted in the final container in which the material is to be sealed under the original vacuum, stored and distributed

The product resulting when serum is subjected to this procedure is a porous solid occupying essentially the same volume as the liquid serum from which it is prepared and this porous product, upon the addition of distilled water, dissolves with remarkable ease and completeness

Remarkably enough, serum so treated suffers no detectable loss in antibody or complement content and, when stored, shows a rate of deterioration only a fraction of that occurring in the liquid state

The use of such preserved complement serum for the conduct of complement fixation (Wassermann) tests in syphilis has been reported upon by several observers Eagle, Strauss, and Steiner, 24 for example, in a study of 3447 duplicate tests in which fresh and dehydrated complement were compared, found no difference in the results obtained and demonstrated, moreover, that dehydrated complement could be kept in the refrigerator for at least ten months without detectable loss of activity

Boerner and Lukens²⁵ have reported upon 12,175 sera and 675 spinal fluids tested with dehydrated complement with results so satisfactory that, because of its greater uniformity and convenience, they have discarded their guinea pig colony

In their experience such complement may be kept in the refrigerator at 464 to 50° F (8 to 10° C) for 12 months without any change in fixability or hemolytic activity. After this deterioration is detected

Personal experience in the writer's laboratory is corroboratory of that noted above and such complement is used as a routine with unvarying satisfaction

The advantages of complement so preserved, while rather obvious, may nevertheless be noted as follows

- 1 Since extremely large pools of complement may be processed at one time and preserved and used over a long period, not only are variations in the fixability and hemolytic activity of the serum from individual pigs nullified, but the product permits greater uniformity than possible with fresh complement
- 2 Preserved complement may be kept on hand at refrigerator temperature, 46 4 to 50° F (8 to 10° C), for as long as twelve months without detectable deterioration
- 3 The necessity of maintaining a guinea pig colony as a source of complement is eliminated

Dehydrated complement may be obtained commercially under the name of lyophile complement. It is supplied in hermetically sealed ampoules containing 5 cc of the dehydrated serum which resembles a buff colored porous solid from which only water has been removed. To restore it to its original state, therefore, all that is necessary is to add five cubic centimeters of distilled water when the material at once goes into solution being then practically indistinguishable from fresh serum in appearance.

It happens, occasionally, that in the conduct of a large Wassermann run more than one ampoule will be needed and some

complement may remain unused Experiments conducted in the writer's laboratory have shown that such unused and, of course, undiluted, complement may be preserved by the addition of sodium chloride, just as fresh complement has been preserved Wastage is thus eliminated.

(To each cubic centimeter of complement serum add 0.3 Gm of chemically pure sodium chloride. Place the salted complement in a stoppered test tube and store in the freezing compartment of an electric refrigerator. For use dilute 1 cc of salted complement with 29 cc of distilled water, thus giving a 1.30 isotonic complement for use in Kolmer's method. Such diluted complement may be added to complement dilutions prepared by adding to 1 cc of dissolved lyophile complement of 29 cc of 0.85 per cent saline solution.)

Lyophile complement when used in large amounts is no more expensive than the maintenance of a guinea pig colony which, as already stated, may be dispensed with

LABORATORY TECHNIC

While toxicological analyses are properly the business of the analytical chemist, the average laboratory, and especially the hospital laboratory is at times called upon to make such analyses as a basis for therapeusis as well as for indicating the necessity for further and more extensive examinations

The methods to follow will be found of service in this connection

A Simple Test for Mercury in Body Fluids and Tissues

Gettler²⁶ describes the following modifications of the Reinsch volatilization test as being rapid, sensitive, and specific

1 To 10 Gm of hashed tissue, stomach contents, or concentrated urine in a 25 cc test tube add 3 cc of concentrated

hydrochloric acid, and place the tube in a boiling water bath.

- 2. Introduce a clean bright spiral of 20 gauge copper wire and allow the tube and contents to remain in the boiling water bath for 30 minutes.
- 3. Remove the spiral and wash it with water, alcohol, and finally ether.

A dark or grayish silvery deposit may be due to arsenic, antimony, bismuth, silver, or mercury. Mercury may be identified by the tests to follow:

- (A.) 1 On a small filter paper placed in a watch glass place a drop of cuprous iodide suspension.* The water in the drop is absorbed, leaving an almost colorless spot of cuprous iodide
- 2 Now cut off the stem of the copper spiral containing the deposit, place the spiral directly on the spot of cuprous iodide, cover with another watch glass, and allow to stand 10 to 15 minutes

In the presence of even a trace of mercury a rose to salmon color develops due to the formation of mercury iodide

- (B) 1 A second copper wire spiral, obtained as described after washing with water, alcohol and ether, is placed in a small (25 multi 075 cm) volatilization tube which is then adjusted through a snug hole in a sheet of asbestos
- 2 Place a microscopic slide over the mouth of the tube and place a small piece of ice on the slide to keep the under surface cool
- 3 With a micro Bunsen flame heat the lower portion of the tube to about 572° F (300° C) for one minute Care must be exercised not to get the upper portion of the tube above the asbestos too hot to keep the slide cold

^{*} Dissolve 5 Gm CuSo4 and 3 Gm of FeSo4 (anhydrous, precipitated with alcohol) in 100 cc of water Dissolve 7 Gm of KI in 50 cc of water and add to the solution just made while stirring Collect the precipitate, wash with water, transfer to a brown glass bottle with the aid of a little water and preserve as a suspension

During the heating any mercury on the slide will volatilize and deposit on the slide as metallic mercury recognizable under the microscope as tiny round silver droplets.

This deposit can be still further identified as mercury by the following procedure Place a crystal of iodine on the slide close to the mercury deposit, cover with a small watch glass, and place the slide (slanted at a 30° angle to the table) in a warm part of the room. The sublimed iodine vapor will run down the inclined slide and on contact with the mercury orange or red mercuric iodide will form, recognizable under the microscope as orange or red rhombic and tetrahedral crystals.

Rapid and Sensitive Test for Fluoride in Body Fluids and Tissues

Gettler and Ellerbrook²⁷ describe the following method for the demonstration of fluoride developed by them in the Chief Medical Examiner's Office of New York City

- 1 Treat 5 Gm of hashed tissue with 5 cc of water and 3 cc of concentiated nitric acid, mix thoroughly and allow to stand 15 minutes when 15 cc of water are added while constantly stirring
- 2 Filter through a Buchner filter with suction
- 3 Add 0.5 Gm of solid lathanum acetate to the filtrate and then sufficient animonium acetate to make the filtrate alkaline to methyl orange A gelatinous precipitate will appear
- 4 Coagulate the precipitate by boiling and filter through a Gooch crucible with an asbestos mat
- 5 Place the mat and precipitate in a crucible and dry on a hot plate
- $6~\mathrm{Add}$ a little powdered glass and and mix

- 7 Add a few drops of concentrated sulfuric acid and immediately cover the crucible with a microscope slide having a drop of water on its under side
- 8. Place the crucible on a heating block at 302° F. (150° C.) and place a small beaker of ice water on the slide to keep it cool
- 9. After three to five minutes remove the slide and add a drop of saturated sodium chloride to the drop of water on the surface of the slide

Hexagonal crystals of sodium fluosilicate develop which, when viewed in a somewhat subdued light, have a slightly pink color.

This reaction will respond to as little as 0.01 mg of fluoride in 5 Gm of tissue

As in acute cases of fluoride poisoning, the urine and stomach contents contain larger amounts than the organs, for such specimens the method may be modified as follows: 1 cc. (1 Gm.) or less, even one drop, of stomach contents or concentrated urine is placed in a porcelain crucible and enough sodium hydroxide solution added to make the reaction alkaline. Dry the material on a hot plate, mix with a little powdered glass, and proceed from step seven above.

Note Human organs usually contain a trace of fluoride (of the order of 0 001 mg in 5 Gm). Therefore two or three crystals may develop from 50 Gm of normal tissue. If only 20 Gm are taken crystals do not form because the sensitivity of the test is not sufficient to respond to the quantity of fluoride present. In cases of fluoride poisoning even ten grams of tissue will give many typical crystals.

The Quantitative Isolation of Alcohol from Tissues

The following method for the quantitative isolation and identification of al-

cohol has been described by Gettler and Siegel 28 and is particularly applicable to medicolegal examinations

The various steps of the method follow

(A) Distillation:

- 1 The tissue immediately after removal from the body is placed in a receptacle which is sealed and refrigerated
- 2 When ice-cold, about 200 Gm. of tissue are finely washed from which 150 Gm are weighed out and placed in a 500 cc distilling flask. In order to avoid appreciable loss by volatilization, these manipulations must be carried out as quickly as possible.
- 3 Add 200 cc of water, 0.5 cc of white mineral oil and set the flask up for distillation
- 4 Pack the receiving flask in ice and collect about 200 cc of distillate. The presence or absence of alcohol can be rapidly established by oxidizing about 2 cc of distillate with a red-hot copper spiral and then testing the oxidized and cooled portion with Schiff's aldehyde reagent. If present proceed with the quantitative isolation to be described.

(B) Quantitative Isolation:

- 1 Transfer the entire steam distillate to the rectification flask shown in the figure
- 2 Immerse the flask in ice water, and while continually rotating the contents, add 200 Gm of K_2Co_3 . The solution should not become too warm
- 3 Now attach the rectification arm to a flask by a ground glass joint and set up the whole apparatus for distillation (The arm is previously cleaned by boiling concentrated nitric acid in the flask and then thoroughly washed and dried)
- 4 Place the rectification flask on an asbestos centered wire gauze and heat with a micro-burner, adjusting the flame so that the solution will boil for 15 to

- 25 minutes without permitting the hot vapors to rise
- 5. Then increase the flame so that within three to five minutes an alcohol ring of condensate arises. The height of the ring is indicated by a visible ring of condensate, or may be determined by running the hand along the arm and testing the temperature. If the rate of heating is correct, the bend should feel warm or somewhat hot, 172 4° F (78° C.) to the hand. This indicates that the alcohol is distilling into the calibrated receiving tube which is immersed in CO₂-acetone mixture.
- 6 After the alcohol has distilled, steam will follow gradually, condense, freeze, and clog up the tube, and therefore, as the heating is continued, back pressure will force the solution up to the safety tube

This marks the end point For large amounts of alcohol the time, from the rise of the first ring of alcohol condensate to the end point, is about 25 minutes

When the rate of heating is too slow the water does not come over but merely condenses and drops back, the arm acting as an air-cooled reflux. In this case, when the actual distillation is not complete after 30 minutes (from rise of ring to endpoint) increase the flame slightly

When the rate of heating is too fast much water comes over before the endpoint is reached. This will be indicated by (a) the bend reaches the temperature of steam, (b) two drops of water are seen to form just beyond the bend although the opening does not become clogged, (c) violent boiling of the solution; and (d) uneven wetting of the sides of the arm

When this occurs the size of the flame should be decreased. It is best, as a rule, to have the flame too small rather than too large, and very important that the

receiving tube be immersed as deeply as possible in the cooling fluid

- 7. When the endpoint is reached (as shown by the solution flowing out of the safety tube, the arm is lifted out of the receiver. The receiving tube containing the alcohol is removed from the cooling bath and allowed to stand at room temperature until any ice present has melted, when the tube is placed in a bath of ice water.
- $8\,$ Add to the alcohol in the tube $0.3\,$ cc of saturated aqueous solution of $K_2\text{-}CO_3$ and some crystals of anhydrous $K_2\text{-}CO_3$ and thoroughly mix for a few minutes with a fine glass rod

If much water has distilled over only the solid K_2CO_3 is added and then stirred for a much longer time (about ten minutes)

- 9 Centrifuge the mixture until a clear layer is obtained (about one minute) and then stand the tube in ice water about three minutes $Excess\ solid\ K_2CO_3\ must$ always be present
- 10 Read the volume of alcohol (upper layer)

Under these conditions (0° temperature and in contact with solid K_2CO_3) the alcohol layer will have the following constant composition

Ethyl alcohol 91 9 per cent K_2CO_3 0 04 per cent Water 8 1 per cent

One cubic centimeter of this (constant composition) layer at 32 $^{\circ}$ F (0 $^{\circ}$ C) weighs 0 833 Gm

Calculation:

One cc of alcohol layer contains $0.833 \times 0.919 - 0.7655$ Gm alcohol

 $0.765 \times cc$ of upper layer = Gm of alcohol in 150 Gm of tissue, or

 $0.5103 \times cc$ of upper layer = per cent of alcohol in tissue

(C) Identification of Isolated Alcohol:

When acetone or paraldehyde are not present in appreciable amounts, the boiling point of the isolated liquid may be determined directly as described below.

Appreciable amounts of acetone are only encountered in advanced diabetes, paraldehyde only when this drug has been administered within 12 to 18 hours before death

If it is desired to obtain 100 per cent pure ethyl alcohol before determining the boiling point, the following method may be used

Micro Drying of Isolated Alcohol.

- 1 With a capillary tube transfer two drops (or more, if available) of the alcohol layer to a larger capillary tube, one end of which is formed into a little bulb, previously filled with finely granulated calcium oxide or anhydrous copper sulfate. The volume of calcium oxide must be larger than the volume of alcohol introduced.
- 2 Centuruge the capillary tube in order to force all the liquid into the
- 3 Seal the open end and place in a boiling water bath for five minutes
- 4 Now place the bulb end of the sealed capillary in the cavity of an aluminum heating block, raise the temperature to 203° F (95° C) and maintain it for five minutes. The alcohol in the bulb distills and appears as a condensate in the cold part of the capillary outside the heating block.
- 5 The part containing the condensate is then centrifuged to force the alcohol to the sealed end
- 6 Take up a small drop by means of a 1 mm bore capillary tube which is then sealed by bringing the tip in the edge of a Bunsen flame for a second Sealing in this way always leaves a bubble of air in the tip of the capillary between the sealed portion of the glass and the drop of liquid which serves to pre-

vent superheating in the boiling point determination

Determination of Micro-Boiling Point.

- 1 Place the capillary containing the drop of liquid in an ordinary melting point apparatus (beaker, liquid bath, thermometer, and stirrer)
- 2 Raise the temperature of the bath slowly and evenly If the drop of liquid in the capillary is pure anhydrous alcohol, it should start ascending at about 1688° F $(76^{\circ}$ C.) and should reach the surface of the bath between 1715 and 1724° F. (775 and 78° C.).

If the boiling point is found to be much lower, 150 8 to 168 8° F (66 to 76° C), it indicates the admixture of lower boiling point liquids such as acetone, or paraldehyde (see above)

The presence of either of these substances can be demonstrated by ordinary qualitative tests

The Detection of C. Welchii in Wounds

The difficulties often encountered in the clinical diagnosis of gas gangrene early in its onset, and the not infrequently indecisive results of bacteriological examinations within the first 24 hours are matters of common experience

In the endeavor to expedite bacteriological diagnosis and to render it more definite Robinson and Stovall²⁹ have restudied this and developed a new method

Perhaps the most frequently cited method for the demonstration of C Welchii is the intravenous injection of rabbits with the suspected material after which they are killed and incubated for 18 to 24 hours. A positive test shows a stormy fermentation of the liver and the presence of a large number of Grampositive, large encapsulated nonmotile bacteria assumed to be C Welchii Unfortunately, because of the frequent, if

not invariable presence in all wounds of a variety of organisms which, for one reason or another, complicate this test, its results are frequently in doubt

The stormy fermentation of milk, also frequently recommended, is not entirely satisfactory in that the characteristic reaction is not always characteristic, and when clear-cut may not appear within the 24-hour period and sometimes not until after incubation for 48 hours. As an early diagnosis is of importance, this test is hence often unsatisfactory.

After an extensive study of the various factors influencing the reaction in milk media, Robinson and Stovall recommend the following procedure for the demonstration of C Welchii as delicate and reliable.

Required 1 Fresh, separated milk tubed in 10 cc portions and autoclaved at ten pounds pressure for 15 minutes on each of two successive days

- 2. Muscle tissue aseptically removed from freshly killed guinea pigs
- 3 Powdered iron sterilized in the dry oven The iron may be kept in small, tightly corked test tubes (1 to 2 Gm per tube) for three to four months

The Method:

- 1 Make Gram and capsule stains and moist preparation and examine for large, nonmotile, encapsulated, Gram-positive bacilli
- 2 Place three tubes of milk in water and heat until the water boils for three to five minutes
- 3. To one tube add approximately 175 mgm of sterile iron
- 4 To each of two tubes add 07 to 08 Gm of fresh muscle tissue One of these tubes serves as a control
- 5 Inoculate the tube containing the iron, and one of the tubes containing tissue with the material to be examined, culturing the swabs directly into the medium if desired

The time required for a positive reaction varies with the numbers of organisms in the inoculum. When stormy fermentation occurs, Gram stains and moist preparations are used to determine the presence of nonmotile bacilli having the morphology of C. Welchii. If present, a positive report may be made

A New Method for the Titration of Antigens for Complement Fixation Tests

As is well recognized, the method of determining the optimum dosage of an antigen for use in complement fixation tests, particularly when applied to the study of syphilis, is of equal importance with the method used in its preparation

The purpose of such antigen titrations is, of course, the determination of the amount to be employed in the test which is capable of eliciting the maximum degree of sensitivity consistent with specificity

The method heretofore in use for the titration of Wassermann antigens is well known but, as has only recently been recognized, is not devoid of possibilities of error arising from various factors among which are certain characteristics related to the interaction between the antigenic extract and the serum used to measure its activity

Because of the varying amount of antibody (reagin) in the serum, as well as because of other factors which need not be discussed here, various observers, among them Eagle, ³⁰ Boerner and Lukens³¹ and Kolmer³² have restudied the question and have thus led to the development of a method of antigen titration which has the definite advantage of being independent of the strength of the positive serum (or sera) used as a measure of antigenic activity

As this constitutes a definite and important advance, the method of titrating

a Wassermann antigen for antigenic activity is given below in detail.

Method .

- 1 In a large test tube or small flask place 01 cc of antigen extract and add 79 cc of normal saline drop by drop, shaking between each addition, thus making a 1 80 dilution
- 2 Prepare from this 1 80 dilution the following

 $4 \operatorname{cc} \text{ of } 1 80 + 4 \operatorname{cc} \text{ saline solution}$ = 1 160

4 cc of 1 160 + 4 cc saline solution= 1 320

4 cc of 1 320 + 4 cc saline solution = 1 640

4 cc of 1 640 + 4 cc saline solution= 1 1280

4 cc of 1 1280 + 4 cc saline solution= 1 2560

3 Arrange five rows of test tubes, six tubes to the row

In the *first* tube of each row place 0.5 cc of antigen 1 80

In the *second* tube of each row place 0.5 cc of antigen 1 160

In the *third* tube of each row place 0.5 cc of antigen 1 320

In the *fourth* tube of each row place 0.5 cc of antigen 1 640

In the fifth tube of each row place 0.5 cc of antigen 1 1280

In the *swth* tube of each row place 0.5 cc of antigen 1 2560

4 Inactivate 3 cc of moderate to strongly positive serum in a water bath at 131° F (55° C) for 15 to 20 minutes and prepare the following dilutions in large test tubes

10 cc + 40 cc saline = 1 5 (05 cc carries 01 cc serum)

0.5 cc + 4.5 cc saline = 1 10 (0.5 cc carries 0.05 cc serum)

0.5 cc + 9.5 cc saline = 1 20 (0.5 cc carries 0.025 cc serum)

20 cc of $1\ 20 + 20 \text{ cc}$ saline = $1\ 40 \ (0\ 5 \text{ cc} \text{ carries}\ 0\ 125 \text{ cc} \text{ serum})$

10 cc of 120 + 40 cc saline = 100 (005 cc carries 0005 cc serum)

- 5 To each of the six tubes in the first row add 0.5 cc of 1.5 serum dilution, to each of the tubes in the second row add 0.5 cc of 1.10, to each tube in the third row add 0.5 cc of 1.20; to each tube of the fourth row add 0.5 cc 1.20; to each tube of the fifth row add 0.5 cc. of 1.40, and to each tube of the sixth row add 0.5 cc of 1.100 serum dilution.
- 6 To all tubes add 1 cc of 1 30 complement carrying two units
 - 7 Prepare the following controls
 - A. Serum control 05 cc 1 10 + 1 cc complement Hemolytic control 05 cc nor-

mal saline + 1 cc complement. 8 Shake the tubes gently and place in the refrigerator at 428 to 464° F

(6 to 8° C) for 18 to 24 hours, followed by ten minutes in a (38° C) water bath

- 9 Add 0.5 cc of hemolysin (two units) and 0.5 cc of two per cent sheep cell suspension to all tubes, mix well, and place in a 100.4° F (38° C) water bath for one hour
- 10 Read the tubes (both control tubes should show complete hemolysis) and chart the results as shown in the example below

example given this would be 0.5 cc of 1.320

If three dilutions give plus four reactions, use the middle or average one as the optimum dose *E. g.*, if plus four reactions are given with 0.5 cc of 1.320, 1:640, and 1.1280 dilutions of antigen, 0.5 cc of 1.640 would be taken as the dose

A Flocculation Test for the Diagnosis of Active Tuberculosis

Rytz and Higgins³³ describe the following simple method as a serologic procedure for the detection of activity in tuberculous lesions which, from a study of 860 cases, seems to have definite value and to be worthy, at least, of more extended trial

Method—1 Obtain blood by venipuncture (or other method) and separate clear serum by centrifugation

- 2 Place 0.3 cc of clear serum in a 10×75 mm tube and place in a 140° F (60° C) water bath for five minutes
- 3 Allow to cool and add 03 cc of alcohol dilution (1 cc of 95 per cent alcohol to three parts of normal saline)
- 4 Shake gently, allow to stand one minute, and then place in a Kahn shaking machine for ten minutes (If shaken

| Serum in | Antigen in 0.5 cc. Amounts | | | | | |
|---|----------------------------|------------------------|----------------------------|---------------------------|---------------------------------|--------------------|
| 0500 | 1 80 | 1 160 | 1 320 | 1 640 | 1 1280 | 1 2560 |
| 0 005 0 0125 0 025 0 05 0 1 | - - + +++ ++++ | - + ++++ ++++ | ++ ++++ ++++ ++++ | - ++++ ++++ ++++ | - ++ ++++ ++++ ++++ | + + ++ ++ |

Determination of Dose—The optimum antigen dose to employ in the main tests is the highest dilution giving a plus four reaction with the smallest amount of serum. If two dilutions give the same dose, use the higher dilution, as recommended by Boerner and Lukens. In the

by hand the rack should make 275 oscillations per minute)

5 Read over a Fisher light for reading Kahn tests, preferably with hand lens

Positive Reaction—Distinct floccules evenly distributed in a more or less hazvifluid

Negative Reaction - Clearer fluid without floccules

Precautions—False positive reactions occur in the presence of colds or pneumonia, becoming negative two weeks after convalescence When old tuberculin has been applied to the skin the test may be weakly or atypically positive for Acute alcoholism may several weeks also produce a false positive reaction which disappears when alcohol consumption is eliminated for several days

In clinically arrested tuberculosis the test is negative and also in severe and hopeless cases

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"OFFICE TESTS" FOR **SYPHILIS**

The mauguration of a nation-wide campaign for the eradication of syphilis has naturally again focussed attention upon this disease in all its phases and, particularly, upon modern methods available for its diagnosis

As is well known, prior to the application in 1906 of the phenomenon of complement fixation to the study of syphilis, the diagnosis of syphilis depended, first, upon the acumen of the physician in detecting in the medical history evidence suggesting the possibility of its presence and, second, upon his skill in demonstrating, by means of physical examination, signs or symptoms corroboratory of this suspicion diagnosis of syphilis was thus largely a matter of clinical skill, entirely dependent upon the physician's familiarity with its varied as well as often bizarre and cryptic manifestations, and also upon the thoroughness of the examination to which the patient was subjected, and finally

upon the physician's ability to detect and recognize the evidences of the disease

The introduction by Wassermann of the complement fixation test as a means of demonstrating the presence of syphilitic "reagin" in the blood and thus diagnosing the disease in the absence of clinically detectable symptoms; and the discovery, soon after, of the Spirocheta pallida with the development of darkfield illumination as a method for its demonstration, completely revolutionized the study of syphilis.

Remarkable as were these achievements in rendering the diagnosis of syphilis, not only more certain but, in many instances, infinitely more easy, it cannot be controverted that, incidentally, they have led to some disregard of syphilis as a clinical problem and to some neglect of the study of its clinical manifestations. For it must be regretfully admitted that, all too often, the study of syphilis consists solely of a Wassermann test and that the diagnosis of syphilis rests mainly upon the report of the test

Insidiously and insensibly there has been some tendency to rely upon the laboratory as the sole arbiter of the presence or absence of syphilis, to drift into the dangerous—though easy—habit of treating, not the disease, but its sero-logic manifestations, and—perhaps most dangerous of all—to regard its management as now reduced to more or less set formulae based upon the newer therapeutic agents available for its treatment

While these tendencies must be recognized they should be strongly decried Particularly is there danger that the publicity attendant upon the syphilis campaign may lead to the impression in the public mind that the Wassermann test, or its equivalent, is all that is necessary to rule out or diagnose syphilis

The syphilis campaign has brought to the fore the flocculation or precipitation

tests developed for the serologic study of this disease and has focussed attention upon them with particular emphasis upon their simplicity of technic and the rapidity with which they may be completed. Indeed, commercial houses have advertised them as simple "office tests" for syphilis requiring practically nothing for their performance but the various reagents, and it is categorically stated that their performance is so rapid, so easy, and so simple that any one—regardless of previous training, or present information—may safely utilize them for the diagnosis of syphilis.

So serious are the implications of these statements, and so gravid with disaster their blind acceptance, that they deserve some comment.

It is true that but little time is required for the completion of flocculation or precipitation tests—but is rapidity the *sine qua non* of the diagnosis of syphilis? Is there any real reason for precipitate haste in the conduct of serologic procedures?

Haste is not mandatory because of danger to the patient by reason of the spread of the infection beyond controllable limits because, if syphilis is to be prevented the preventive measures must be instituted within at most two hours after exposure when neither lesion nor serologic manifestations are present, and, moreover, the treatment of syphilis can never be limited to any definite time, regardless of when it is initiated

It cannot be because the delay, even of days, is unwarrantedly dangerous in the known or suspected syphilitic for the treatment of the disease is a tedious affair at best

Syphilis is not a disease in which life, death, or ultimate care is a matter of hours or days. Efficient treatment is a matter of years and while it is true that, the earlier treatment is begun, the

better the ultimate expectations, a delay even of days is a matter of little moment in the last analysis. In the early case, by the time the serology is positive, the disease has spread beyond local limits; in the late case, or one discovered years after insufficient treatment, a further short delay before starting treatment again is of relatively little moment.

The specificity of a serologic procedure is far more important than the rapidity with which it may be completed -in competent hands and with adequate safeguards—the flocculation tests are reliable, delicate and useful adjuncts in the serologic study of syphilis has been thoroughly established by the painstaking studies of a host of investigators same studies, however, have also shown that, as is true of any reaction dependent upon the interaction between the patient and his disease, the flocculation tests have their limitations and in their interpretation may be influenced by a variety of factors

It is true that flocculation tests are technically more simple than complement fixation tests and require less time, less labor, and less apparatus for their performance. But this simplicity, in a sense, is more apparent than real Behind their simple manipulations are the same basic principles underlying the complement fixation test—principles none of which are simple, all of which are complex, and some of which are even yet incompletely understood

Mere knowledge of the technic of flocculation tests is insufficient for their safe application to the serologic study of syphilis unless backed by a thorough training and understanding of serologic methods in general. For there is no serologic method which may not go awry—even in skilled hands—and the worker must be both fundamentally trained and

thoroughly experienced, not only to appreciate when trouble begins, but especially to find and eliminate the cause

It is of practical importance to emphasize that in the hands of the average worker—due chiefly to the personal factor involved in the reading of the reaction—false doubtful and false positive reactions occur in direct proportion to the skill and experience of the worker How much greater will be such findings in the hands of the unskilled and untrained!

Furthermore, it should not be lost sight of that extensive investigations have conclusively demonstrated that no serologic procedure, no matter what its nature or how great its specificity and sensitivity, can be accepted as invariably correct in its results. There is not—nor can there ever be any method of serologic examination which can be regarded as "fool-proof" nor the results of which can be taken purely on their face value

Serologists and syphilographers recognize this fact just as they realize the many factors-too many and too complex to be discussed here-which are responsible for it, and it is for this reason that one serologic procedure should be fortified and checked by another of equal value, and for this reason a complement fixation and a flocculation test simultaneously performed upon the same person far outweigh in clinical value and utility, the results of either alone For, regardless of the skill with which these tests may be applied, certain proved syphilitic sera give consistently negative reactions to flocculation tests and consistently positive reactions with complement fixation tests and vice versa, so that, in such instances, the presence of syphilitic reagin can only be detected when both tests are used And, finally, flocculation tests are not yet generally applicable to spinal fluid with consistently satisfactory results

Few dicta are more important than this. The LABORATORY PROCED-URE IS NEVER AS IMPORTANT AS ITS INTERPRETATION!

It is important that the public be informed as to the danger of regarding the "blood test" as the *ultima thule* of the study of syphilis. No more dangerous doctrine could be spread, and if it is spread, and if "blood tests" are to be done indiscriminately by those unfamiliar with the pitfalls surrounding these complex procedures, it is inevitable that many a potential focus of infection will be missed on the one hand, and many a patient labeled with the undeserved stigma of syphilis on the other on the basis of some "rapid" and "simple" test in unskilled hands

The old adage may well be reiterated Be quick to suspect syphilis but slow to diagnose it! The words of James Gregory, Professor of Medicine in the University of Glasgow from 1790 to 1821 are pertinent, indeed, and may well be recalled with profit:

"I do not know, nor can I conceive, any human contrivance that can more effectually and irresistibly oblige the physician to study carefully the case of his patient; to attend to every symptom and change of symptom, to exert himself to the utmost for his patient's relief and, at the same time, to be as careful as possible in the remedies he employs; than to find himself under the necessity of giving a minute account of everything he has done in a very public manner and before a number of competent judges"

Under such circumstances there might well be some embarrassment attached to a diagnosis of syphilis based upon a ten-minute test and ten cents' worth of reagents'

PEDIATRICS

Edited by A Graeme Mitchell, M D

ANEMIA IN CHILDREN

By Clare R Rittershofer, AB, AM, MD

Introduction—Further studies have been made of the anemia of prematurity, among them being the work of H Mackay, who suggested that premature and immature babies whose general health and progress have been satisfactory from birth do not usually show any severe anemia during the first three months of life In an attempt to further define the anemias of the newborn, Cohen has classified them in two groups, one showing many nucleated red cells and marked jaundice, the other no early forms of erythrocytes and pallor instead of jaundice Parsons and Smallwood have pointed out that the anemia of scurvy probably results from a slowing down of the whole process of blood formation. In chronic cases a posthemorrhagic blood picture may be superimposed The treatment of nutritional anemia has largely resolved itself into the administration of iron preferably in a ferrous form Copper is no longer considered a necessary adjunct Splenectomy in sickle cell anemia continues to suggest a favorable line of therapy as judged by the results several vears after treatment

The entire subject of anemia of infancy and early childhood has been carefully reviewed by Hugh W Josephs ¹

Definition of Anemia—Anemia is defined by R L Haden² as a reduction below normal of the capacity of the blood to transport the oxygen necessary for all animal life

Mechanism of Anemia—The same author amplifies this definition by point(910)

ing out that the hemoglobin normally present (15 to 16 Gm per 100 cc of blood) increases 100 times the power of the blood to transport oxygen by carrying it in chemical combination If this amount of hemoglobin were in solution in the circulating blood it would increase the osmotic pressure of the plasma beyond that of the surrounding tissues and so dehydrate the tissues But since hemoglobin in a red cell is outside the plasma, it does not affect the osmotic pressure, and it functions efficiently as an oxygen carrier since absorption and release of oxygen is as efficient as if the hemoglobin were in solution in the plasma

In order to evaluate the formation, circulation, and destruction of red cells, certain indicators of red cell activity are necessary The red cell count and the hemoglobin content record only the balance between red cell formation and The number of red cell destruction reticulocytes present is an index of the rate of production of red cells or at least the rate of delivery from the marrow The marrow may be hyperplastic or hyperactive with a low reticulocyte count in the circulation if the delivery of cells from the marrow is impaired On the other hand, if the reticulocyte count in the circulation is high, the marrow is necessarily hyperplastic, if below normal, the marrow may be aplastic, hypoplastic, or hyperplastic

When a red cell is destroyed, hemoglobin is set free, iron is split off from the hemoglobin molecule, and bilirubin

| RELATION | OF | BLOOD | FORMATION | AND | DESTRUCTION | то | BILIRUBIN | AND | RETICULOCYTE LEVEL |
|-------------|----|-------|--------------|------|-------------|----|-----------------|------|---------------------|
| TOPPETATION | O. | DLCCD | T OWNER TOTA | **** | DESTRUCTION | 10 | T2 YTTY C T2 T1 | TILL | TOTTO CHOOL THE THE |

| Bilirubin Content | Reticulocyte Count | | | | | |
|------------------------------|---|--|--|--|--|--|
| (icterus index) | Increased (over 15%) | Normal (0 5-1 5%) | Decreased (under 0 5%) | | | |
| Increased (over 6 units) | Increased blood destruc- tion with active bone marrow | Increased destruction without good marrow response | Increased destruction with inactive bone marrow or impaired delivery of red cells | | | |
| Normal (4-6 units) | Active bone marrow without excessive destruction | Decreased marrow with- out excessive destruc- tion of red cells | Decreased formation or impaired delivery of red cells without excessive destruction | | | |
| Decreased (under 4 units) | Decreased destruction of hemoglobin due to iron deficiency, active cell formation in mar- row | Decreased destruction of hemoglobin. De- creased formation of hemoglobin, normal cell formation in mar- row | Decreased destruction of hemoglobin Decreased formation of hemoglobin Decreased cell formation in marrow or impaired delivery of cells. | | | |

is formed as the end product of the pigment metabolism. Bilirubin thus formed is not easily excreted by the kidney or by the liver cells, so that excessive destruction of red cells and hemoglobin is shown in an increased bile pigment content of the plasma. A correlation of the bilirubin content of the plasma and the reticulocyte level is shown in the above table by Haden

The two specific elements, iron and erythrocyte maturing factor, otherwise known as "antianemic principle of Castle," the "pernicious anemia principle," and "antimegalocyte principle," are necessary if the marrow is to make a normal cell with a normal complement of hemoglobin The fundamental action of the latter is to mature the red cell or prepare it for emergence from the marrow The cell to which this substance or erythrocyte maturing factor is supplied becomes smaller so a decrease in volume of the cell is characteristic of the maturation effected by the erythrocyte maturing factor and a macrocytosis is indicative of its lack. Iron is the specific element necessary for normal red cell formation Iron is necessary for the formation of hemoglobin and

probably stimulates the growth and multiplication of red cells at the normoblast stage where division is most active With a decrease in the normal amount of hemoglobin in the blood, there is first a decrease in the concentration of hemoglobin in the red cell or decreased color index If the color index continues low, the cells become smaller and the volume index decreases The hypochromia shown by the lessened color index and volume index is a measure Indicators which of the lack of iron show these various relationships are given in the following table

MEASURES OF RED CELL ACTIVITY

| Factor | Indicator | | |
|---|--|--|--|
| Balance of red cell and hemoglobin forma- and destruction | Red cell count and hemoglobin content | | |
| Rate of destruction of red cells | Level of bile pigment in plasma | | |
| Rate of regeneration of red cells | Level of reticulocytes in circulation | | |
| Deficiency of iron | Hypochromia and mi- crocytosis of red cells | | |
| Deficiency of erythrocyte maturing factor | Macrocytosis of red cells | | |

PEDIATRICS

Since an anemia represents a loss of balance between red blood cell formation and destruction, an anemia can result only from increased blood loss without a compensating increase in blood formation, by decreased formation with a normal or accelerated blood loss, or by a combination of increased blood loss and decreased formation

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Anemia of the Newborn

E J Huenekens³ reported a case of anemia of the newborn in which improvement followed immediately after intramuscular injection of liver extract and suggested that future cases of this disease be subjected not only to clinical tests of liver therapy, but also to specific tests for the presence of the intrinsic factor formed by the mucosa of the The use of liver in anemia of the newborn is based on the hypothesis that in this condition there is a temporary absence of the antianemic principle of Castle When a pregnant woman fails to secrete a sufficiency of this substance for both herself and the fetus, one of two things may happen either the infant receives more than its share, causing macrocytic anemia of pregnancy, or the mother retains the major portion of the antianemic principle, causing anemia of the newborn

The treatment of three cases of anemia of the newborn with severe jaundice with human blood serum has been reported by G H Krost ⁴ He points out that this form of therapy was first advocated for cases of icterus gravis neonatorum by Hampson in 1928 and 1929 Two of the three infants reported by Krost showed no erythroblasts in their stained sinears while the third had an increased number. All three infants were deeply jaundiced but only one had an enlarged spleen. No family history of jaundice was present in any

of them The infants were treated by daily injections of 10 to 12 cc of blood serum for one, three and four days, respectively. Marked improvement in the general condition followed thereafter

Acute Hemolytic Anemia of Lederer

W. H Patterson and G S Smith⁵ described a case featured by a verv acute onset, pyrexia, a rapidly progressive anemia, the evidence of hemolysis as shown by the typical skin coloration and the van den Bergh reaction, the high reticulocytosis and the presence of normoblasts and megaloblasts indicating active erythropoiesis, the negative blood culture and absence of any discoverable form of infection, and the complete arrest of the hemolytic process by a single blood transfusion Lederer first described the condition as acute hemolytic anemia in which there was definite evidence of blood destruction of unknown etiology and a liability to a fatal issue in the absence of blood transfusion

Congenital Hemolytic Anemia in Infancy and Childhood

In congenital hemolytic icterus and spherocytic jaundice the red cell mechanism, according to R L Haden (loc cit), reveals a well marked anemia with a high icterus index (15 or more units), indicating excessive blood destruction and a high reticulocyte count showing good marrow response The bone marrow is hyperactive The fundamental difficulty in this disease is an anatomic defect in the shape of the red cells which are spherocytic rather than normal biconcave disks As a result of this abnormal shape, the cells are more fragile than normal and are rapidly removed from the circulation by the spleen which is enlarged as a result of the increased activity More iron and bilirubin than normal are poured out Here the average length of life of the red cell is a few days instead of the usual thirty days. There is a rapid stream of cells from the site of origin, the bone marrow, to the place of destruction, the spleen The anatomic defect can not be corrected but the patient is treated by removal of the spleen, the destroyer of the fragile cells The abnormally shaped cells function normally if allowed to remain in the circulation. The anemia. reticulocytosis and jaundice all disappear after splenectomy, showing that the increased activity of the spleen is the cause of the anemia although the fundamental defect is in the bone marrow

L K Diamond⁶ points out that the chief characteristics of congenital hemolytic jaundice are A chronic or recurring type of anemia associated with relatively mild interest becoming accentuated during crises of hemolysis, splenic enlargement, increase in amounts of urobilin in the urine and stools, increased fragility of the erythrocytes in hypotonic salt solutions, elevation in percentage of reticulocytes in the circulation out of proportion to the degree of anemia present, and a tendency for the red cells to be microcytic and globular

These features may be more marked in the young as, for example, the jaundice may not be so prominent a symptom, whereas the anemia may become so severe, especially during crises of hemolysis that death may result from lowering of the red cell and hemoglobin levels and subsequent anoxemia. Infants and children in general are more sick than jaundiced. The spleen may become so enlarged as to fill the whole left side of the abdomen, the anemia is profound, the cells show more tendency to variation in shape, the reticulocytes may rise to tremendous percentages, and the fragility

test may show hemolysis beginning in normal isotonic saline solutions

Other symptoms are the frequent occurrence of severe abdominal pain accompanied often by vomiting and some fever during the hemolytic crises of the disease in childhood The differential diagnosis of congenital hemolytic anemia from an acute surgical condition may be difficult, especially if jaundice is not too prominent and if the blood picture is not appreciated. Besides the usual findings characteristic of the disease there may be evidences of interference with bodily function due to recurrent anemia, such as marked cardiac enlargement with cardiac decompensation

X-rays may show retardation in growth and late appearance of centers of ossification as well as marked thinning of the cortices of the bones of the extremities with increase of the medullary portions The latter may be the result of the hypertrophy of the marrow tissue in an effort to keep up red cell production Continued hyperbilinubinemia in unoperated cases may lead to the production of gallstones and the subsequent danger The author from biliary obstruction stresses the point that the younger the patient at the time of the first crisis of hemolysis, the more severe the disturbance tends to become Death may occur during an attack, even during the first, and a hemolytic crisis may be quickly followed by all the symptoms of acute and fatal hemorrhage Early splenectomy for these cases is indicated Splenectomy controls the tendency to hemolytic crises and relieves the burden placed on the heart by the chronic and recurrently severe anemia

One complication that must be watched for is the building up of a tremendous platelet level within the first week or two following operation. This may be associated with evidence of intravascular

thrombosis, manifesting itself in abdominal pain, fever, leukocytosis and even convulsions The "platelet crisis" usually subsides in a relatively short time.

Iron Deficiency Anemia

Chlorosis-This condition was formerly regarded, according to C. W. Heath,7 as one of the earliest forms of anemia to be recognized as a clinical entity. It was considered as an anemia of adolescent girls, without definite etiology, responding well to iron medication A large number of factors were cited as possible etiologic agents In 1934, L S P Davidson and I Leitch⁸ commented on the causative factors in chlorosis by saying that "although described as a primary anemia in all textbooks of medicine, there can be little doubt that chlorosis was essentially a nutritional anemia, consequent on deficient iron intake" Today chlorosis in severe form is uncommon and as such is diagnosed very rarely Nevertheless, a mild hypochromic anemia responding to iron occurring in adolescent girls is quite common, and severe hypochronic anemia is occasionally seen The author points out that a diet poor in iron can not be responsible alone for non deficiency Iron loss of some sort other than metabolic loss of iron in the urine and stools must occur At the time of puberty there is an acceleration of growth This, together with the demands for menstrual loss of blood in girls, produces an annual iron requirement which is proportional to the requirement for a normal pregnancy It is apparent, therefore, that an iron deficiency can result in girls after puberty if one of a number of factors are upset The normal factors are Normal growth and menstruation, a healthy appetite, a good diet and a healthy gastrointestinal tract Abnormal factors which may condition an iron deficiency are Abnormally rapid growth, excessive menstruation or bleeding elsewhere, a diet poor in iron or poor appetite, and such gastrointestinal disorders as achlorhydria and prolonged diarrhea

Nutritional Anemia - This is the term used to designate a type of anemia found most commonly in infants from six months to two years of age believed to be due to lack of stores of 1ron in the body The disease frequently occurs in infants whose diets have consisted largely of milk, although it may develop in those whose diets include cereals, vegetables, eggs and beef broth H W Fullerton.9 in discussing the iron deficiency anemias of infants from the ninth month to the end of the second year, points out that the etiology of this type of anemia may be considered under four headings (1) Type of milk feeding, (2) effect of maternal iron deficiency, (3) birth weight, and (4) the effect of infections From the age of five months onward the average hemoglobin levels of the breast-fed infants were higher than in those who received "mixed feeding," and considerably higher than in "bottle fed" infants

The author also concluded that his results failed to show any significant correlation between the common degrees of material iron deficiency and anemia in late infancy, and the iron content of the newborn infant is probably independent of that of the mother except, perhaps, in the most severe degrees of maternal iron deficiency Also that the anemias of premature infants and twins is a direct consequence of two factors—a low iron content at birth and rapid growth Further. that the common infective illnesses of infancy produce a rapid fall in hemoglobin level and may inhibit blood regeneration for a considerable time after the disappearance of clinical evidence of

Other factors which might play an etiological rôle were achlorhydria, low

blood volume and low dietary intake during the second year. It ought to be emphasized that anemia should be explained on the basis of deficient iron intake only in cases where the birth weight was normal, and where no infections have occurred, and it should be borne in mind that severe anemia due to dietary deficiency alone is unlikely to occur during the first year The author recommends the use of medicinal iron in preference to dietary measures, and a hemoglobin determination of all infants at three months Where such a procedure can not be carried out, a course of iron therapy should be given routinely at the age of three months to all infants of birth weight less than seven pounds, and in cases of artificial feeding Iron therapy should be started after illnesses of an infective nature, and should be continued for at least two or three months

Incidence — A study of 290 patients admitted during two years to the Princess Elizabeth of York Hospital for Children was made by L Findlay¹⁰ in an effort to determine, if possible, whether nutritional anemia is common among the poorer-class children of the East End of London The striking feature of the in vestigation was that for the most part the red cell and hemoglobin determinations fell within the range of the physiological, and therefore did not suggest any great incidence of anemia of a nutritional type or any other variety

Blood Picture—G M Guest and E W Brown¹¹ have directed attention to the fact that the alteration of the size and hemoglobin content of the red cells is a more exact criterion of anemia in infants than is the hemoglobin level of the blood. Infants with hemoglobin values below 10 Gm usually can be recognized clinically but those who have between 10 and 11 Gm often go unrec-

ognized. Blood samples were obtained at intervals of approximately three months from a large number of patients who were studied from birth through their early years in an attempt to define the normal and abnormal limits of variability of the red cell count, the mean red cell volume, the hemoglobin content of the whole blood and the hemoglobin content in each cell in order to determine what constitutes borderline anemia. By this method of study borderline anemia was found to occur much more frequently among seemingly normal infants than is generally recognized.

The significant changes in addition to the drop in the hemoglobin level were diminutions in cell volume indicating a microcytosis and a low mean hemoglobin content per cell. The diminution in the size of the cells occurs earlier than the decrease in the hemoglobin concentration. and both depress the mean hemoglobin content per cell For clinical purposes, a hemoglobin content of 20 micromicrograms or less per cell justifies a diagnosis of anemia regardless of the hemoglobin content of the whole blood Iron therapy in the form of a 12 per cent solution of iron and ammonium citrate, given in doses of 3½ minims per pound (05 cc per kilogram) of body weight was sufficient to bring about a rapid increase in the size of the cells as well as in the hemoglobin concentration per cell and the hemoglobin content of the whole blood

R L Haden (loc cit) in an explanation of the mechanism of this type of anemia reports that the marrow is hyperplastic in an attempt to compensate, but such red cells as do emerge are small and deficient in hemoglobin. The low volume and color index indicate the iron deficiency. In this case there is less destruction of hemoglobin so very little iron is set free and the bile pigment of the plasma is less than normal

Iron Retention-F W Schlutz, M Morse and H. Oldham¹² studied three anemic infants, 13, 8 and 8 months old respectively in an effort to determine the effects of certain foods on their iron retention All three infants were in a positive iron balance and each showed consistent weight gains during every period studied Puréed spinach apparently was not utilized by the infants When apricots were fed the retention of iron showed a slight increase in all cases, perhaps due, as the authors suggest, to the fact that a much higher percentage of the iron of apricots than of spinach is in the inorganic form Iron salts, when given in large doses either in the form of ferric ammonium citrate or ferrous sulfate caused a marked retention of iron and an increase in the hemoglobin value Cupric sulfate, when given with either a high or low iron intake, did not produce any additional increase in the iron retention or in the hemoglobin level The ferrous salt did not seem to have any advantages over the ferric salt. There was no evidence that liver was of any value in the treatment of the secondary anemia of these infants, either when fed alone or in addition to a diet containing spinach, apricots and iron and copper salts

Iron versus Iron and Copper Therapy—C A Elvehjem, D Duckles and D R Mendenhall¹³ have compared the effectiveness of iron alone with iron fortified with copper in treating the same anemic patient and concluded that iron alone stimulates a slight increase in the formation of hemoglobin but the response is inadequate in that the hemoglobin level does not reach the average figure for healthy infants (11 5 to 12 5 Gm per 100 cc of whole blood) On the other hand they found that iron supplemented with copper causes a maximum response in raising the hemoglobin

The solution of iron used was ferric pyrophosphate prepared by dissolving 247 grains (16 Gm) of powdered ferric pyrophosphate in 133 ounces (400 cc) of distilled water containing five per cent of alcohol One teaspoonful (4 cc) was the daily dose equivalent to 3/8 grain (25 mg) of elemental iron For the iron and copper solution, 5 grains (032 Gm) of copper sulfate was added to the iron formula previously mentioned This is equivalent to $\frac{1}{60}$ grain (1 mg) of copper to 3/2 grain (25 mg) of iron to be the most satisfactory To them it seems dangerous to administer large doses of iron since animal experiments have pointed to the fact that excess iron interferes with the assimilation of phosphorus and may produce rickets The copper content of the blood in pigs suffering from nutritional anemia has been studied by M O Schultze, C A Elvehjem and E B Hart¹⁴ and has been found to fall to extremely low levels Feeding $\frac{1}{30}$ to $\frac{1}{15}$ grain (2 to 4 mg) of copper per day together with iron results in a very rapid and significant increase of the copper content of the blood, but when small amounts of copper were fed together with iron the increase in the copper content of the blood is only small and hematopoiesis is slow. The authors suggested that rapid, continued hematopoiesis can not take place unless the copper content of the blood is maintained above a minimum level. It has been demonstrated by the same authors¹⁵ that the unavailability of copper in naturally occurring food materials and compounds that might be used for copper therapy is not a problem of practical importance as far as the dietary supply of copper is concerned

Iron Therapy—W B Castle¹⁶ states that the administration of iron is essential In general the ferrous compounds

are more effective per gram of iron than ferric compounds Roughly 12 grains (0777 Gm) of ferrous sulfate, 30 grains (194 Gm) of reduced iron or 60 grains (388 Gm) of iron ammonium citrate administered daily are efficient doses. Elixir of ferrous sulfate is a convenient means of giving iron to children I F Brock¹⁷ points out that the treatment of the hypochromic anemias with large doses of iron has been very encouraging and that the specificity of iron therapy has only been generally accepted since these preparations have been used in large doses. It has been quite clearly established that the hypochromic anemias are conditioned, mainly, if not solely, by a state of iron deficiency, and that they can not respond properly to any form of therapy which does not supply enough iron to be incorporated in the new hemoglobin A rise of hemoglobin of from one to two per cent per day is considered a satisfactory response to iron and this represents the addition to the circulation of from 35 to 1 grain (23 to 64 mg) of iron Since preparations on the market contain less than $\frac{1}{20}$ grain (3 mg) per dose, their use is decidedly inadequate The author points out that some cases of hypochronic anemia respond well by supplying about 1 grain (64 mg) of iron daily by mouth for new hemoglobin and for the replenishment of other nonhungry tissues in the body Other cases respond only when iron is given in doses of 3 grains (200 mg) daily rational explanation of the necessity for such large doses has been provided At present there is no way of distinguishing clinically those cases in which small amounts of 110n are adequate and those which require larger doses The average optimum dose of iron and ammonium citrate is 60 to 90 grains (4 to 6 Gm) a day, and of Blaud's pill 45 to 90 grains (3 to 6 Gm) Tablets of ferrous sulfate

should be given in doses varying from 15 to 30 grains (1 to 2 Gm) daily. If ferrous chloride is used in a syrup solution an average optimum dose varies from 9 to 18 grains (0 58 to 1 16 Gm.) a day (at least 4½ grains or 300 mg of metallic iron) according to whether the ferrous chloride is anhydrous or not

Two prescriptions for iron solutions¹⁸ are given below

- Referred ammonic citratis 3vi (24 Gm)

 Syr. limonis 51 (30 cc)

 Glycerini 5ss (15 cc)

 Aquae q s ad 5vi (180 cc)

 Sig Two teaspoonsful three times a day.
- R Ferri et ammonii citratis 3ii (8 Gm)
 Aquae q s ad 3iv (120 cc)
 Sig One teaspoonful in three of the baby's
 bottles
- J C. Sharpe¹⁹ points out that the prophylactic administering of iron to infants during the first two months does not prevent or alter the occurrence of physiologic anemia
- C W Heath (loc cit) recommends the following preparations in the treatment of chlorosis Ferrous sulfate, 12 grains (0.77 Gm), iron and ammonium citrate, 92 grains (6 Gm) daily, reduced iron, 30 to 60 grains (2 to 4 Gm) daily Prophylactic doses of iron at puberty were one pill a day containing ferrous sulfate—3 grains (0.19 Gm) or one teaspoonful of iron and ammonium citrate scales dissolved in milk daily

Sickle Cell Anemia

E A Sharp and E M Schleicher²⁰ in a study of three patients with sickle cell anemia, noted that the bone marrow cell counts were slightly above normal Observations on natural and induced changes in peripheral blood and bone marrow preparations demonstrated that the sickling trait of the erythrocytes can be overcome by washing in saline and reinduced by addition of the patient's

blood serum Sickling occurred in bone marrow cells of sickle cell anemia when sealed in normal serum from an individual of the same blood type. Blood cells from a normal individual of the same blood type retained their normal contour when in contact with serum from a case of sickle cell anemia for a period of six days. The offspring of a patient showing a severe sickle cell anemia did not manifest the sickling trait immediately after birth

R L Haden (loc. cit) points out that in sickle cell anemia there is a fundamental defect in the marrow with the delivery of cells of abnormal shape and probably with a greater tendency to fragment The marrow is overactive as shown by the reticulocytosis, and the red cell destruction is excessive as shown by the increased icterus index spleen is enlarged early in the disease due to overactivity in removing excessive numbers of abnormal cells from the circulation Splenectomy helps the anemia but the patient continues to have some anemia after removal of the spleen. The increased cell destruction and formation also continue so the excessive activity of the spleen can not be the sole cause of the anemia. It is most probable that the red cells fragment more easily than normal and this fragmentation continues after splenectomy There is no treatment for this phase of the disorder Splenectomy removes only one factor

() C Hansen-Pruss²¹ has shown that supravital staining with janus green, bril-

liant cresyl blue and methylene blue or treating with one per cent sodium cyanide accentuates the tendency and accelerates the process of sickling in red cells possessing the sickling trait. It is probable that sickling is activated by the dyes by producing a condition of more or less profound anoxemia in the red cells. With the use of the dyes mentioned, it was found that 12 per cent of an unselected group of 100 negroes showed the sickle cell trait, as contrasted with a reported average of about six per cent in groups of negroes where moist unstained preparations were used.

W P Killingsworth and S A Wallace²² studied 60 cases of sickle cell anemia without anemia. They express doubts as to whether there is a true asymptomatic phase of sickle cell anemia. The anemic phase may show the clinical picture of rheumatic fever, tuberculosis, syphilis, acute abdominal conditions and obscure anemias.

Cooley's Anemia

R S Cuizza²⁻³ reports that 20 months after splenectomy performed on a three-year-old child ill with Cooley's anemia, the child showed marked improvement without any apparent change in the fundamental process

Rickets and Anemia

K B McDonough and D R Borgen²⁴ were unable to demonstrate a significant difference in the hemoglobin content of the blood of normal and rachitic chicks

CHICKENPOX

By Robert A Lyon, AB, AM, MD

The occurrence of other diseases simultaneously with an attack of chickenpox often greatly increases the severity of the latter infection. An instance in which

diphtheria occurred with chickenpox in a patient six years of age has been described by J W Healy ²⁵ Diphtheria was contracted first and was followed in

two days by the appearance of the vesicular eruption of chickenpox The fluid within the vesicles became hemorrhagic, which the author believed to be due to the circulating diphtheria toxin The severity of the diphtheria infection was evidenced by petechiae of the skin and edema of the fauces and periglandular tissue The patient seemed to be recovering from the hemorrhagic form of chickenpox when he suddenly died, apparently of cardiac failure Other instances of hemorrhagic chickenpox which have been described in the literature includes those associated with sepsis, scarlet fever, purpura, and other toxic and infectious diseases

The prevention of chickenpox in susceptible children exposed to the disease by use of convalescent serum was found to be of little value by J M Lewis, L H Barenberg and G Grossman ²⁶ Ten cc of the serum were administered intramuscularly to 23 children on the first to third day after exposure to chickenpox, while a control group of 18 children in the same wards received no treatment. The disease developed in 91 per cent of the treated group and in 95 per cent of the control series. The convales-

cent serum was a pooled lot which had been obtained from 20 children, about two weeks after the onset of the illness. The majority of previous reports had upheld the virtue of chickenpox convalescent serum as a protective substance but the authors were unable to agree with those conclusions

An advocate of a definite relationship between varicella and herpes zoster is K. Kundratitz.27 From the reports in the literature and from his own observations and experiments he believes that the two diseases have a similar or identical background He has been able to immunize patients against varicella with the use of vesicular material obtained from zoster patients Similarities between the two infections are (a) the character of the individual lesions, (b) the appearance of the elementary bodies of each and (c) similar agglutination reactions Such differences as the variations of complement fixation reactions were thought to be due to (a) imperfect technic, (b) the differences in symptoms and (c) age distribution, (d) slight variations of the strain of virus or (e) differences in types of allergic response of individuals

DIABETES MELLITUS IN CHILDREN

By Waldo E Nelson, AB, MD

The relation of vitamin B_1 to diabetes mellitus has been discussed Experimental deficiency of vitamin B_1 results in a disturbance of the carbohydrate metabolism characterized by a rise in the blood sugar and in the glycogen content of the liver and muscle. In diabetes, while there is an increase in blood sugar, there is a deficiency of liver glycogen. Thus it does not appear that deficiency in vitamin B_1 is a causative factor in the

production of diabetes mellitus. However, in those instances when the diet is deficient in vitamin B_1 the diabetes may be aggravated and conversely administration of vitamin B_1 may result in a partial improvement of carbohydrate tolerance

It was pointed out that so-called renal diabetes may be characterized by intermittent as well as by continuous glycosuria, the glycosuria depending on the

renal threshold, which in the three instances reported was 60 mg. per cent, 135 mg per cent and 155 mg per cent, respectively A report of a case of galactosuria was also reviewed Removal of milk from the diet resulted in the disappearance of sugar from the urine

Protamine Insulin

Satisfactory and somewhat similar experience with *protamine insulin* in the

and Dummer found it to be the exception rather than the rule that their patients were able to be maintained in satisfactory glycemic equilibrium on a single morning dose of protamine insulin However, satisfactory control was obtained in practically all instances when a small dose of regular insulin was given in the morning in addition to the injection of protamine insulin It should be remembered that injections of protamine insulin and

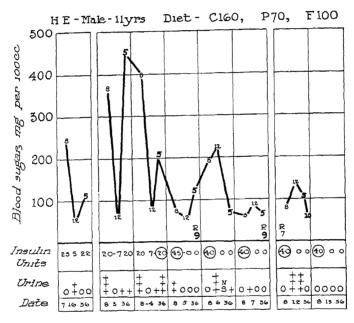


Chart 1—Satisfactory results from one injection of protamine zinc insulin per day (Courtesy, Journal of Pediatrics, April, 1937)

treatment of diabetes mellitus in children has been reported by A L Newcomb, M W Dick and L Schnute²⁸ and by W E Nelson and C M Dummer ²⁹ Newcomb and his co-authors state that children with mild diabetes can be treated satisfactorily with a single morning dose of protamine insulin. In the case of severe diabetes, they have found that a majority of the children can be adequately controlled by a simultaneous administration of a large dose of protamine insuline and a smaller dose of regular insulin before breakfast. Nelson

regular insulin must be made separately and in different sites. In transferring a diabetic child from regular insulin to protamine insulin, Nelson and Dummer state that it is their practice to establish reasonably satisfactory glycemic equilibrium with regular insulin and then to administer the first dose of protamine insulin in an amount equal to that of the regular insulin, at the time of the evening meal. By this method the blood sugar of the following morning is usually within the normal range and the slowly acting protamine, which is then admin-

istered in the morning, does not have to overcome the additional burden of an existing hyperglycemia (See Chart 1).

The first morning injection of protamine insulin consists of approximately the total daily requirements of regular insulin, or slightly less, according to the plan suggested by Sprague and his assowhich was sufficient to lower adequately the level of blood sugar after the noon and evening meals, the child was quite likely to have a hypoglycemic reaction during the night or early morning hours On the other hand if the amount of protamine was adjusted so that the blood sugar of the following morning was

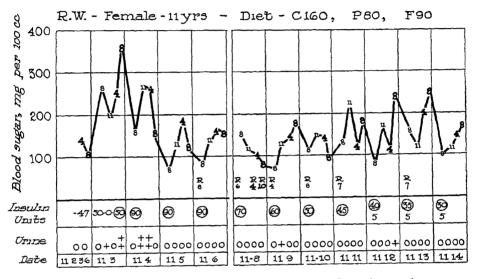


Chart 2—Combined use of protamine zinc insulin and regular insulin (Courtesy, Journal of Pediatrics, April, 1937)

KEY TO CHARTS

Graph The figures indicate the hour at which blood samples were collected, light face numerals represent A M and dark face P M "R" signifies insulin shock, the numeral the hour of occurrence

Insulin Plain numerals represent units of regular insulin, numerals enclosed in a circle, protamine insulin, and those in a square, crystalline insulin

Urine, qualitative Benedict tests O = blue, + = green, + = greenish yellow to yellow,

+ and + = orange through red

In Chart 1 the urine was collected at 800 A M , 12 noon, 500 P M and 900 P M , and in Chart 2 at 800 A M , 1100 A M , 400 P M and 800 P M

All blood examinations were made on capillary blood (Courtesy, Journal of Pediatrics, April, 1937)

ciates Subsequent adjustments of dosage are made in accordance with the level of the blood sugar and the amount of urinary sugar. When necessary to control the mid-day blood sugar, regular insulin is administered at breakfast time in addition to the protamine insulin. In general it was found that when an amount of protamine insulin was given

within the normal range, the blood sugar levels during the day of administration were likely to be high. An example of the procedure followed in procuring satisfactory adjustment is shown in Chart 2. In regard to the subjective reactions of the children, Newcomb and his coworkers report that the children did not experience periods of intense hunger, that

they were more active and alert and those who received all of the insulin in the morning were happier and more stable emotionally

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Both groups of authors point out that although hypoglycemic reactions tend to be less frequent and less severe with protamine insulin than with regular insulm after the child is properly regulated, insulin shock does occur from protamine insulin and may be quite severe. The onset of hypoglycemic reactions from protamine insulin tends to be slower and more insidious than after the injections of regular insulin If these mild symptoms are disregarded, however, the child is likely to develop very severe Furthermore, because of the shock longer continued effect of protamine insulin, several shocks may result from a single injection. Thus, the child may have a second, or even a third reaction after satisfactory treatment of the initial shock It is important to instruct the child and his family concerning the nature of these reactions When large doses of protamine insulin are given at breakfast time, the hypoglycemic reaction is most apt to occur from 12 to 24 hours after the injection, many of the reactions occurring in the early morning hours, or at approximately breakfast tıme

H R Drysdale³⁰ has been able to maintain satisfactory control of ten juvenile diabetics on protamine insulin administered once a day, before breakfast and without the aid of supplemental doses of regular insulin. Some of the children required additional injections of regular insulin, administered before breakfast, for several months, but after this time it was possible to discontinue the regular insulin entirely. Marked subjective improvement was reported by all of the children in contrast to their experience with regular insulin. The initial

dose of protamine employed by the author was an amount of protamine equal to the combined number of units of regular insulin previously administered over a 24-hour period. In several instances it was necessary to give a greater number of units of protamine than had been given of regular insulin. In most of these instances, however, the children had not been perfectly controlled with regular insulin.

Relation of Insulin Dosage to Increase of Weight

H J. John³¹ has attempted to determine whether there is any relation between the insulin requirement and the weight increase in diabetic children. Although in general he found that the insulin requirement increases with growth, this was not invariably so and even in those who required an increase in insulin dosage no fixed rule could be determined for estimating the increase in dosage. The author emphasizes the important point that each diabetic child must be treated individually in regard to the dietary prescription and the insulin needed to balance it

Local Reactions Due to Injection of Insulin

An instance of *lipomatosis* in insuliningected areas in a diabetic boy is reported by G B Bader and F Vero ³². As is the case with lipodystrophy, lipomatoses occur in areas where repeated insulin injections have been given over a long period of time. The clinical appearance seems to be much the same in all the reported instances. There is an absence of inflammatory reaction. The subcutaneous tumefactions have a lipomalike, soft consistency and the adherent skin is stretched and slightly thickened. There is often a pronounced hypoalgesia of the skin in these areas. This phenomenon is

apparently secondary and is due to repeated traumatization of the fine sensory nerve endings. No serious sequelae have been observed to date and the lipomatous process appears to be benign. There is no known therapy, but a definite reduction in size may be noted when further injections in the area are avoided. The frequency of lipomatosis is probably greater than the reports in the literature would indicate. The Reviewer has himself observed two such cases in some forty diabetic children.

In the treatment of insulin atrophy, J A. Shelly³³ emphasizes the fact that prevention is of the greatest importance All diabetics should be cautioned to rotate the site of injections. The author instructs his patients to use the inside of the thigh, the outside of the thigh, the inner and outer aspects of the arms, both sides of the abdomen, the buttocks, and under the shoulder blades, in rotation Such a plan will lessen the possibility of overstimulation in any one region as well as insure adequate rest for each part He also advises the use of the higher concentrations of insulin, believing that the decreased bulk of the injection lessens the possibility of mechanical trauma Particular care should be taken with younger children since they seem to be especially susceptible If atrophy has occurred in any location, further injections should not be made at this site, even though the evidence of atrophy has disappeared When atrophy occurs, Shelly employs physiotherapy in the form of gentle stimulation, such as light massage, galvanic current and, in the more severe cases, heat in order to produce hyperemia

Blood Lipids

The observations of I L Chaikoff, F. S Smyth and G E Gibbs³⁴ indicate that the blood lipid levels of diabetic

children, when controlled by insulin and diet, are well within the normal range This was found to be so for all lipid constituents, i.e., free and esterfied cholesterol, phospholipids and fatty acids. Normal lipid values were found when the diabetes had been present for from three months to three years and in children who required from 10 to 68 units of ınsulın per day Three diabetic children were studied during mild acidosis. In no instance during acidosis was the cholesterol content of the blood found to be significantly above the highest normal A distinct lack of relation between cholesterol and the total fatty acid was noted Thus, cholesterol cannot be employed as a guide for the level of other lipid constituents in the blood.

Treatment of Newly Born Infants of Diabetic Mothers

Pregnancy among diabetic women has increased materially since the introduction of insulin This has created not only the problem of caring for the diabetic woman through pregnancy but also that of caring for the newly born infant who is apt to develop hypoglycemia. The latter is presumably the result of the overactivity of the pancreas of the fetus during the latter portion of pregnancy The infants of diabetic women also tend to be large at the time of birth, making the labor more difficult. For these reasons, L M Randall and E H Rynearson³⁵ advocate delivery by Caesarian section in the 36th or 37th week of pregnancy.

The authors have developed a general plan for the management of the infant of the diabetic mother for the first few days of its life. They state that the length of time that the program will need to be maintained will vary and will depend on the degree of prematurity, the length of time before food and fluids can be

taken by mouth and the duration of the period of readjustment of pancreatic function The blood sugar of the mother, the infant and the umbilical cord should be determined immediately. It is preferable to obtain separate samples from the umbilical artery and vein pharynx and trachea should be freed of any mucus and amniotic fluid which may be present If necessary, carbon dioxide and oxygen may be administered to establish respiration After respiration has started, the infant is placed in a Hess incubator equipped with a cover and connected with an oxygen tank The flow of oxygen is regulated to maintain an oxygen tension of 40 to 50 per cent for the first few hours The temperature of the incubator is maintained at 85° F (295° C)

Five cc of a ten per cent solution of dextrose is administered in each buttock Further injections of 10 cc of a ten per cent solution of dextrose are given as indicated by the level of the blood sugar, by the behavior of the infant and by the ability of the infant to take feedings by mouth Feeding is attempted within four hours Ten ce of a ten per cent solution of dextrose or 7 cc of Marriott's lactic acid-Karo mixture is given every two hours for the first 48 hours if it is tolerated Then 30 cc of the lactic acid-Karo mixture is given every three hours. The infant should be under uninterrupted observation for the first 48 to 72 hours Whenever the feeding is poorly taken or whenever twitching, convulsive movements or cyanosis indicate the development of hypoglycemia, 10 cc of a ten per cent solution of dextrose is given by mouth, if possible, otherwise intramuscularly The length of the period of danger from

hypoglycemia cannot be predicted The concentration of oxygen in the incubator is diminished gradually, and when the infant maintains normal color in the ordinary atmosphere, the administration of oxygen is discontinued

Non-diabetic Glycosuria

An instance of glycosuria resistant to insulin in which the glycosuria could be markedly decreased by the substitution of levulose or lactose for dextrose in the diet is reported by H H Mason and G E Sly 36 The child had a low fasting blood sugar, however, an abnormal rise in blood sugar and glycosuria followed the ingestion of dextrose, while the injections of isocaloric amounts of levulose or galactose or large amounts of protein or fat caused much less rise in blood sugar and little or no glycosuria There was little or no response to insulm The authors believe that the difficulty was in the storage of dextrose in the liver, since the capacity for metabolising levulose and galactose was greater than for dextrose. They also believe that there must be some difference in the mechanism of storage of levulose and galactose as opposed to dextrose It is suggested that all monosaccharides including dextrose are converted into glycogen or to some other intermediate product and then reconverted to dextrose It is suggested that the difficulty in this instance was in the ability of the liver to convert dextrose to glycogen or some other intermediary product and was not a pancreatic deficiency. In support of this hypothesis, the child gained weight on a diet in which the carbohydrate was supplied daily in the form of galactose and levulose and without insulin

DIGESTIVE SYSTEM

By Waldo E Nelson, AB, MD

Mouth

There is a distinct lack of agreement concerning not only the efficacy of various medicaments in the treatment of Vincent's stomatitis but also in the need for treatment other than the practice of good oral hygiene. For this reason the experience of G. W Farrell and W A McNichols³⁷ is of interest, since they had the opportunity to evaluate various forms of treatment in an epidemic, occurring in an institution in which 794 cases were treated In contrast to those authors who feel that treatment other than simple oral hygiene is unnecessary, Farrell and McNichols noticed that the manifestations of the disease became more acute the longer they were allowed to progress without treatment. In this series, the severity of the disease appeared to be determined by the resistance of the patient and the virulence of the affecting organisms Adults and children of low mental development were particularly susceptible

The authors believe that thorough prophylaxis and scaling of the teeth, accompanied by the removal of all mechanical irritations, is as necessary in the treatment of Vincent's stomatitis as the use of drugs However, they emphasize the fact that the slightest surgical procedure, even in the presence of mild degrees of infection, should be avoided Various drugs were used in different groups of patients during the epidemic However, the authors felt that the proper use of hydrogen peroxide, U S P, was the prime factor in curing Vincent's infection In some instances they felt that benefit was obtained from the use of other medicaments However, they state that one cannot be sure of a cure unless hydrogen peroxide is used in addition. They did not observe any reaction which suggested that it could be used to excess. A full strength solution was employed at least four times a day and in some instances recovery seemed to be hastened when it was employed more frequently, for example, every two hours. The authors do not believe that the intravenous use of the neoarsphenamine is of value in the treatment of this infection.

Pyloric Obstruction

The possibility of an hereditary factor in pyloric obstruction of infants is raised by T. Halbertsma ³⁸ In the support of this argument he reports seven instances occurring in three families, two of which were closely related A familial tendency has also been noted by E Brendle ³⁹

It is emphasized by A F Hartmann⁴⁰ that successful treatment of pyloric stenosis depends not only on the type of treatment given, but also on the early recognition of this condition and on the proper preoperative preparation and postoperative care. In recent years practically all of the patients admitted to the author's clinic have been operated upon The mortality has varied inversely with the percentage of patients treated surgically The technic of operation employed has been that of Fredet-Rammstedt Satisfactory preparation for operation included (1) relief of dehydration and alkalosis and partial restoration of glycogen reserves, (2) restoration of plasma protein content and red blood cell volume and (3) control of infec-Ringer's or lactate-Ringer's solution is administered subcutaneously to relieve dehydration and alkalosis. dextrose to abolish ketosis and restore the

glycogen reserve (a ten per cent solution given intravenously) and citrated whole blood (intravenously) to restore plasma protein and red blood cells

The author's routine for post-operative feeding is as follows (1) two hours after operation ½ oz of sterile water or 10 per cent buffer water* is offered, and two hours later 1/2 oz of a formula or breast milk if available The author employs a formula consisting of equal parts of evaporated milk, 20 per cent buffer water and sterile water to which is added enough carbohydrate in the form of Karo syrup to provide a final addition of four to five per cent During the first 24 hours, formula and water administration are continued alternately every four hours, the volume of each is kept at ½ oz During the next 24 hours the quantity of each is raised to 1 oz, during the third day to $1\frac{1}{2}$ oz with subsequent gradual additions until after one week, the buffer solution can be discontinued and the usual one per cent lactic acid diluent substituted The formula may also be more concentrated by omitting all or a part of the sterile water

Control of persistent vomiting in infants by roentgen ray therapy is reported by R. A. Higgons, T. West and M. Durvee 41. The authors have treated ten infants by this method with the relief of vomiting in all instances. Their procedure is as follows a suitable formula is prescribed and atropine or luminal or both are given before each feeding. If the vomiting is not relieved in from 24 to 48 hours, x-ray therapy is given. The amount of radiation necessary is appar-

ently quite small In the earlier cases, those which first attracted the attention of the authors, the only radiation given was that amount necessary for fluorscopic examination of the stomach and for the making of one or two negatives In the ten cases included in this series. approximately 60 to 100 r units were given over the dorsal spine and corresponding paravertebral area The factors used were nine inch gap (115 kv.); 5 MA, 10 inch S T distance, 3 mm aluminum filter, 1 to $1\frac{1}{2}$ minutes' time If there is a definite improvement in symptoms, no further treatment is given If, however, the vomiting increases again after a period of improvement, the roentgen ray treatment is repeated In no instance have the authors found it necessary to administer more than two treatments. It is the author's belief that the roentgen rays act in some manner upon the pyloric spasm and that this is the most probable cause of the vomiting in the infants in this series

Cyclic Vomiting

C H Smith⁴² in a discussion of the causes and treatment of recurrent or cyclic vomiting states that this symptom complex is a definite clinical entity which is seen more often in private than in hospital practice in this country. The children usually come from families whose members are high strung, of above average intelligence, and in which there is a definite family tendency to migraine, cyclic vomiting and prematurely gray hair, especially on the maternal side A number of children with cyclic vomiting later have migraine in adolescence or young adult life and some become gray before they are 30 Smith also believes that the effective treatment of both conditions with sedatives or analgesics also points to the conclusion that the recurrent vomiting is a childhood equiva-

^{*} Concentrated buffer solution has the following composition

U S P lactic acid (75-85 per cent) 150 cc 10 per cent sodium hydroxide 200 cc Water qs 1000 cc

A ten per cent buffer water is a 1 10 dilution of this concentrated solution

| TABLE I | | | | | | | | | | |
|------------|---------|-----------|------------|----|-------------|--|--|--|--|--|
| RELATION O | F FLUID | THERAPY T | о Symptoms | OF | DEHYDRATION | | | | | |

| SYMPTOMS | PROBABLE CAUSES | TREATMENT | | |
|---|---|---|--|--|
| Lessened Turgor of skin and | Loss of fluid from blood and tissues | Saline solutions | | |
| Sunken Fontanel, etc | | Saline and Dextrose solutions | | |
| Oliguria or Anuria Cyanosis | Impaired Circulation (Concentration and decreased volume of blood) Dehydrated Tissue Tissue Acidosis | Saline and Dextrose solutions Saline solutions | | |
| Abnormal breathing | Acidosis (low blood CO ₂ and pH) or Alkalosis (high blood CO ₂ and pH) | Saline and (if severe) Alkali Saline and (if severe) Acid | | |
| Convulsions | Acidosis Alkalosis or | Saline and Alkali Saline and Calcium | | |
| Acidosis (low blood CO ₂) | Guanidine Intoxication Loss of Base (by diarrhea) (Na and K) Tissue Anoxemia Impaired Kidney Function | Saline and Calcium Saline (if severe) calculated amount of sodium as bicarbonate or lactate | | |
| Alkalosis (high blood CO ₂) | Loss of Chloride (by vomiting or diarrhea) | Saline and Calcium (if severe) Acid as HCl | | |

lent of migraine It is pointed out that while ketosis occurs during the attacks, it has not been proved that it is the cause of the vomiting Treatment of the ketosis with rectal or intravenous glucose is said to have no effect on the vomiting, and ketosis may be disregarded except in the neglected patients who have been vomiting for several days. The author advises the administration of bromides by rectum, and of codeine which he says will abort most attacks within a few hours In the intervals between attacks the child is permitted a full, nourishing diet and there is no restriction of fats The child should be spared fatigue and excitement as much as possible by providing extra rest periods and a carefully planned daily régime

Gastroenteritis

The importance of replacement of fluids to correct the dehydration of enteritis as well as of specific treatment for acid base disturbances in this condition are emphasized by G E Cullen 43 It is stressed that dehydration from acute gastroenteritis is not only a symptom which indicates the severity and duration of the loss of water, but in itself may so change the physiologic balance of the body that it becomes of greater danger to life than the initial cause of the disease It should be recognized that loss of fluid from the body, either through vomiting or diarrhea, not only draws water and various salts from the blood but also draws water and salts from the tissues, and that because of the

TABLE II OUANTITIVE ASPECIS OF FLUID TREATMENT

| Quantitive | ASPECIS | OF | FLUID | TREATMEN' | Г |
|------------|---------|----|-------|-----------|---|
| | | | | | _ |

For Emergency Intravenous Treatment

Either 09% salt or any Modified Ringer's Solution equal volume with 10% dextrose = 5% dextrose

If Acidosis

If Alkalosis

Between 25 and 40 vol % CO₂ Calculated amount of either Sodium Bicarbonate or 1/6 Molar Lactate

Below Over 9

Below 25 vol % CO₂ Calculated amount NaHCO₃ Over 90 vol % CO₂ Calculated HCl in Saline and

5 cc 10% Calcium Gluconate

Calculation of Bicarbonate Dosage

g = b x wt (kilos) x 0.026 Where g = grams NaHCO3 needed

 $b = deficit (65 - determined CO_2 content in vol \%)$

i e, 1 gram NaHCO3 per Kilo weight raises CO2 content about 40 vol %

Example wt 10 K CO2 content 15 vol % $10 \times 40 \times 026 = 10$ grams NaHCO3 = 200 cc 5% NaHCO3 solution *

Calculation of Acid Dosage

cc concentrated HCl = vol % CO_2 excess (over 70) x 0028 x wt (kilo) Acid added to 09% NaCl Never more than 5 cc concentrated acid per 100 cc Saline Stop if hyperpnea develops

Never inject acid or alkalı faster than 3 cc dilute solution per minute

For continuous Treatment

Total fluid (by mouth and parenterally) not to exceed 2½ to 3 oz per pound per day Physiological salt solution to be replaced by "plasma salt solution"

loss, there may result a general acidosis or alkalosis In general, voniting, with excessive loss of gastiic contents, without diairhea, causes an alkalosis because of the loss of hydrochloric acid Whereas excessive loss of fluid from the upper intestinal tract without vomiting results in the loss of base, sodium and potassium, with consequent acidosis Between these two extremes there are, of course, many combinations in which both chloride from the stomach and base from the intestines are excreted in such abnormal quantities as to lower the body store When possible, fluids should, be of course, be given by mouth However. in extreme instances of dehydration or when vomiting is persistent, fluids must be replaced parenterally in adequate amounts. Acid or base therapy should not be employed unless quantitative data of blood analyses are available and then the quantity should be determined by means of the formulae illustrated in Table 2.

Apple Powder—The use of apple powder as a substitute for fresh apple in the treatment of acute and chronic disorders of the intestinal tract is recommended by R de Rohan Barondes 44 Among the advantages noted are its availability at all times, a more accurate mixture with milk or water can be obtained than with watery and variable apple pulp; the powder may be readily mixed without causing coagulation or

^{*} Raising the CO2 to 55 is sufficient. The factor 40 is thus obtained (55-15=40)

curdling as is frequently caused by apple pulp, the powder does not undergo oxidation with the resultant brown color. and the product remains standard and stable Clinical experience indicates that it is as efficient as apple pulp in controlling diarrheal conditions. The apple powder is usually given in a four to eight per cent suspension of boiled water No sugar is added Each mixture should be freshly prepared for each administration by adding the requisite amount of apple powder to the hot water, 104° to 122° F (40° to 50° C), and then allowing it to stand for five to ten minutes during which time it should be shaken several times

A substitute for scraped apple in the treatment of diarrhea of infants has been described by M Winters and C A Tompkins ⁴⁵ This preparation consists of

Dextrin and Maltose 175 grams
Pectin 6 grams
Agar-Agar 8 grams

This formula is based upon the theory that the two active principles in apples so far as therapy in diarrhea is conceined are pectin and cellulose dextri-maltose is added as a source of calories The three ingredients are mixed in the dry state and will keep for an indefinite period. The dry mixture containing the above amounts of the separate ingredients is added to a pint of milk or water The water or milk is boiled with the pectin-agar mixture over an open flame for from three to five minutes While still hot it is poured into eight custard cups This constitutes a day's feeding on a three-hour schedule If the substitute has been made with water the total number of calories is 700, if it is made with whole milk, 1020 If less fat is desired, skimmed milk may be used The mixture may be made more palatable by such flavors as vanilla, chocolate or fruit and various colorings may also be added Flavoring is unnecessary for infants and small children, but for older children this constitutes a simple means of preparing an attractive and tasty therapeutic food. The feeding may be made more concentrate or dilute by using powdered milk or by decreasing or increasing the amount of liquid

The authors have compared the therapeutic effect of this pectin-agar mixture with that of apple therapy by placing alternate cases of diarrhea on one or the other of these two preparations They present data to show that the group treated with the pectin-agar mixture responded better than the group fed scraped, raw apples The following advantages in the use of the pectin-agar mixture are noted The diarrhea is more rapidly controlled and gain in weight is greater. The pectin-agar mixture is more readily taken by the infant and the preparation is more adaptable to various dilutions and concentrations and the carbohydrates, fat, protein and vitamin contents may be altered as desired The original cost is less than that of apples and there is less likelihood of waste The pectin-agar mixture may be more easily prepared and the prepared gel keeps indefinitely in the icebox Apples cannot be given in a sterile condition, whereas the pectin-agar mixture is easily kept sterile after preparation The pectin-agar mixture may be available at all times whereas suitable apples are not

The experience of the Reviewer would indicate that the large amount of dextri-maltose might be reduced in this pectin-agar mixture

Successful employment of *banana therapy* in diarrheal diseases in infants and children is reported by C. L. Joslin ⁴⁶ An immediate and appreciable reduction

in the number of stools and a tendency to prevent weight loss was noted in both dysenteric and nondysenteric diarrhea. When banana powder or ripe banana was employed in the treatment of typhoid fever, no appreciable influence was noticed except in cases accompanied by diarrhea For the treatment of diarrhea in infants, the dehydrated banana powder proved very effective, whereas in dysentery and typhoid fever in older children, the raw fruit was more efficacious

The usual plan of therapy was an initial period of starvation (water alone for 24 hours) with administration of parenteral fluids and then feedings of one of the banana preparations, initially only in a mixture with water for 24 hours and then in combination with protein milk, fat free Bulgarian buttermilk or boiled skimmed milk amount of banana powder varied from three to six tablespoonfuls in 24 hours It was usually added in amounts corresponding to the quantity of carbohydrate given in a day's feeding When fresh bananas were employed, fully 11pe fruit was chosen, that is, the pulp was soft and the peels flecked with brown The fruit was mashed and put through The minimal number a fine sieve administered per day was two whole mashed bananas, the maximal five, depending upon the age of the child

Duodenitis

Two instances of duodenitis occurring in children are reported by I R Jankelson ⁴⁷ The author is in agreement with those who believe that duodenitis not only accompanies a duodenal ulcer but frequently precedes it and is a predisposing factor in its formation. He does not imply, however, that duodenitis must terminate in a duodenal ulcer, although he suggests that duodenitis in childhood may be the precursor of duodenal ulcer.

in adult life and that the best prophylaxis against the later development of a duodenal ulcer is the early recognition and proper treatment of duodenitis in childhood

The clinical manifestations of duodenitis in a general way resemble those of a duodenal ulcer Pain, if present, is most apt to be in the upper part of the abdomen and may radiate to the back or chest The pain may be of a gnawing or burning character but is rarely sharp and is often related to the intake of food, reaching its maximum severity from one to three hours after meals Alkalıs relieve pain to a lesser degree in duodenitis than in duodenal ulcer Fullness and distress, soon or several hours after meals, may be the only complaint Nausea, belching and heartburn are common Vomiting is not a frequent symptom However, hemorrhage, both gross and occult, is common and may be the first and only symptom Perforation of the duodenum has not been reported in association with duodenitis without an accompanying ulcer Determination of gastric acidity has not revealed constant findings The most important evidence for the diagnosis of duodenitis is obtained by roentgenographic examination Even this may not be characteristic and diagnosis must be made mainly by exclusion The common identgenographic findings are as follows. There is an inconstant deformity of the duodenal cap without a maiginal niche or a central fleck The duodenum is irritable, it fills indistinctly and empties rapidly. The bulb is usually small and grossly deformed and the deformity varies quickly from moment to moment The cap lacks density and the margins may be hazy The mucosal pattern is coarsely and irregularly recticular The stomach frequently shows active peristalsis and increased tone There is often transient pylorospasm, but the presence of gastric residue after six hours is rare.

The treatment of duodenitis is the same as that of a duodenal ulcer Rest, a carefully graded diet, elimination of foci of infection and administration of alkalis in doses sufficient to neutralize the stomach contents but not large enough to produce alkalosis, are the accepted factors in treatment When a child is given a first stage Sippy diet, with its excessive fat content, ketone bodies frequently appear in the urine Their presence, however, need not produce anxiety. since when the second stage diet, with its increased carbohydrate intake, is given, the ketosis disappears Surgical intervention is seldom justified

Colitis

In an excellent review of chronic ulcerative colitis in childhood, H F Helmholz⁴⁸ lists the factors to be considered in the differential diagnosis They are (1) the typical history of a bloody diarrhea with much mucus and pus, (2) the glazed or granular appearance of the rectum and sigmoid flexure, as seen by proctoscopic examination, (3) the smooth, lead pipe appearance of the colon as seen in the roentgenogram after administration of a barium enema, (4) the isolation of the diplococcus of Bargen (this organism was isolated in 75 per cent of the author's cases), and (5) the absence of other bacteria or parasites usually associated with dysentery The recognition of the condition is not difficult if the symptom complex is known It appears to be the rule, however, that this condition typically goes unrecognized for many years In the author's series of 65 cases, the majority had had their symptoms for more than one year before the diagnosis was made

The treatment of chronic ulcerative colitis consists of rest in bed during the

acute and subacute stages. All foci of infection should be removed if possible. The diet should be of the low residue type but high in vitamins and calories If there is great loss of fluid from the intestines, fluids should be given intravenously. During the chronic stage, the character of the diet does not seem to have much effect upon the type of stools, and much harm may be done by restricting the diet largely to carbohydrate foods Vitamins in the form of brewer's yeast, fruit juices and cod-liver oil should be given in adequate amounts. Iron in large doses is indicated to combat the anemia Transfusion of blood is a valuable procedure In a number of instances, the author states that improvement seemed to date from the time of the transfusion When the blood count is normal, a number of small transfusions of from 150 to 250 cc of blood may give striking results in reducing the number and changing the character of the stools Colonic irrigation with various antiseptic solutions are not employed Various drugs, such as paregoric, tincture of opium, kaolin and subcarbonate of bismuth, have been used to control the diarrhea Administration of tincture of iodine in doses of 5 to 10 minims (03 to 06 cc) three times a day has proved helpful in some instances The specific serum introduced by Bargen has proved distinctly beneficial, but apparently has not been so effective as in the treatment The serum is administered after the patient has been desensitized One tenth of a cubic centimeter is at first administered twice a day, and the dose is increased gradually to several cubic centimeters The dose should be kept within the limits of local or general reactions Results are observed in from two to three weeks After improvement has taken place, increasing doses of vaccine, beginning with 01 cc, are ad-

ministered Even when there is a continued improvement, it is advisable to repeat the vaccine treatment three or four times a year

Relapses have occurred with great frequency, and it is quite evident that the disease is very chronic and persistent and that it is likely to flare up with any infection or lowering of resistance which results from fatigue or exposure.

Celiac Disease

C W Ross⁴⁹ has studied the glucose tolerance of children with celiac disease, chronic intestinal indigestion and abdominal tuberculosis. In such patients he has demonstrated the association of a flat, oral glucose tolerance curve with a high intravenous one. He believes that this indicates a deficient power to absorb carbohydrates from the intestines. He has also shown that the administration of liver extract, either enterally or parenterally, tends to improve the glucose tolerance where it is impaired in these conditions.

Appendicitis

In a study of the case records of the Willard Parker Hospital, J G M Bullowa, E. J. McCabe and S. M. Wishik⁵⁰ have found that appendicitis occurred more frequently as a complication of varicella (0.19 per cent of 2534 cases) and of measles (017 per cent of 6357 cases) than of the other infectious diseases studied, namely, scarlet fever, diphtheria, pertussis, poliomyelitis and other disorders (0.02 per cent of 70,571 cases) It is stated that the syndrome of pseudoappendicitis in the prodromal stage of measles may be more common than is generally recognized, and it may lead to unnecessary and untimely operative treat-Symptoms simulating those of ment acute appendicitis often occur at the end of the incubation period, just at the beginning of the catarrhal invasion of the upper respiratory tract At this same period, specific histopathologic changes are present in the appendix, in the form of collections of giant cells in the mucosal and submucosal layers In the eruptive period, appendicitis is not a rare occurrence, and at this time early perforation and extensive tissue necrosis are the rule The appendiceal involvement is usually not recognized before perforation since attention is focused on the respiratory and cutaneous aspects of the measles It is pointed out that abdominal symptoms associated with the exanthems, especially measles and varicella, should always suggest the possibility of acute appendicitis (See SMALLPOX and MEASLES)

That food allergy may be a cause of abdominal pain and should be considered in the determination of the causative factors is pointed out by J II Fries and G A Merrill 51 They state that abdonimal pain of allergic origin may arbitracily be divided into three types (1) Severe abdominal pain simulating an "acute surgical abdomen", (2) abdominal pain of subacute recurrent nature, and (3) abdominal pain as a minor symptom Important factors in the history include a family history of allergy, a past history of some other type of allergy, a previous history of gastroenteric symptoms or a sensitivity to specific toods. The diagnosis is confirmed by the use of "trial diets"

The ideal therapy is the elimination of the offending food. However, it may not be possible to determine the specific food or there may be such a multiplicity of causative foods as to make it impracticable to avoid them all. The authors have not been successful in the employment of oral desensitization. They have obtained the most satisfactory results with acid therapy. Dilute hydrochloric acid. (U.S.P.) is prescribed in doses of

½ to 1 dram (2 to 4 cc) three times daily in fruit juice (sweetened if desired) or in cold water Belladonna and atropine as well as catharsis have been of doubtful value. Their experience with ephedrine has not been sufficient to evaluate it properly.

Typhoid Fever

Treatment — K Habel and W Crocker⁵² have had the opportunity of treating typhoid fever in 19 children who were simultaneously infected All of the children received high caloric diets. Six of them were treated with intramuscular injections of specific immune human serum with no marked effects Five of the very ill children were given nonspecific immunotransfusion therapy with immediate marked improvement which was followed by recovery authors are not willing to evaluate this latter form of treatment because of the small number of children treated However, they believe that it promises to be a helpful form of treatment Their plan for the preparation of the donor is as follows A suitable donor is selected on the basis of his general health, negative serology, and satisfactory typing and cross agglutination He is hospitalized and 50,000,000 killed typhoid bacilli are given intravenously The usual stock typhoid or mixed typhoid, paratyphoid A and B

vaccine, 1,000,000,000 organisms per cc. is used, of which ½0 cc is the dose. If the donor does not have a reaction within an hour, the dose is repeated Usually within an hour after injection of the killed organisms, the donor has a chill followed by a rise in temperature to from 102° to 104° F. (39° to 40° C.) and leukocytosis up to 25,000 This reaction continues for an hour or more, but the temperature returns to normal within a few hours Eight hours after the injection of typhoid vaccine, the donor's blood is taken. It is given to the patient by the direct or indirect method in two transfusions of from 100 to 200 cc on two successive days Five hundred cc of blood are drawn from the donor and that which is not used in the first transfusion may be kept safely in the icebox for 72 hours

The typhoid vaccine is not given to the donor with the idea of stimulating the production of specific antibodies against the typhoid bacilli, but rather as a means of producing a foreign protein reaction Presumably, the donor's cells are stimulated to a maximum production of opsonins or other nonspecific immune bodies are transferred from the donor to the patient as a form of passive immunity and they presumably affect the bacteria in such a way that the leukocytes of the patient may readily phagocytize them

DIPHTHERIA

By ROBERT A LYON, AB, AM, MD

The classification of the bacteria in this disease into three general groups, of gravis, initis and intermediate types, has been made according to their appearance and fermentation reactions. The gravis and intermediate types were usually isolated from severe diphtheritic infections, while the mitis types were obtained from milder clinical infections

Alum precipitated toxoid continues to be used successfully for mass immunization of children Older children and adults are more apt to develop severe local reactions and even systemic distuib-

ances Two doses of alum toxoid seem to be more effective than the single injection methods, using 01 or 02 cc as an initial dose and 04 cc as the second dose three to four weeks later

Simultaneous immunization against diphtheria and smallpox has been accomplished in a group of 100 children without any reactions and with the development of 95 per cent negative Schick reactions and 95 per cent successful "takes"

In the treatment of diphtheria carriers, a three per cent solution of methyl violet has been used with success, instilling one drop in each nostril and painting the tonsils twice a day for periods of eight days

Incidence — The annual report of diphtheria deaths occurring in 93 large cities of this country indicates a decline of mortality rates in all geographical locations 53 The New England section continued to have a good record with death rates very similar to those of the previous year The group of cities of the middle Atlantic states had the lowest rates (0.65 deaths per 100,000 population) and the highest figures were reported by the cities representing the south central group of states such as Louisiana. Texas and Oklahoma, although even here the rates were reduced from 5.58 in 1935 to 4.39 in 1936. The total number of diphtheria deaths in all the cities during the year of 1936 was 584, of a population of more than 38 million, or a rate of 152 per 100,000 population This is the lowest figure ever attained, and may be compared with a rate of 209 in 1935 and 94 ten years previously in 1926 It seems very probable that antidiphtheria immunization has played an important part in the reduction of the diphtheria mortality in this country Many deaths reported by cities in the

above groups represent nonresidents who possibly have not been reached by immunization campaigns

A review of diphtheria mortality statistics in the cities of London, Manchester and Glasgow, by R M F Picken, 4 indicated a shifting of the preponderance of the deaths from the preschool to school age groups. In the past, the programs of immunization have been conducted primarily for children one to five years of age because of the severity of the illness at that period of life. The author believed that it was now necessary to direct further efforts towards the immunization of the children of early school ages.

Bacteriology-Variations in clinical types of diphtheria infections have been attributed to different strains of diphtheria bacilli, classified as gravis, mitis and intermediate types. The investigations of M Gundel⁵7 of 10,000 strains of diphtheria bacilli obtained from 2058 patients indicated that in a certain number of patients, 954 of the entire group, the clinical course of the disease could be determined by the type of bacilli found Of the patients with gravis types of bacıllı, 46 per cent had mıld clınıcal courses and 13 per cent had severe infections, a higher percentage of severe cases than in the group with mitis or intermediate types of bacilli Of 60 severe diphtheria infections, 54 were due to gravis types of bacilli Large doses of antidiphtheritic serum did not seem as effective in combating severe infections as the early administration of the serum The distribution of types of bacilli among clinical cases of diphtheria and among carriers seemed to be about the same Any changes in the type of bacillus carried by a single individual seemed to result from an invasion of another type rather than any change in the bacilli already present in the nose and throat

K. L Pesch⁵⁶ was able to classify diphtheria bacilli obtained from 2610 carriers and patients in different stages of their diphtheria infections. Of 332 different strains obtained, three general classes of gravis, mitis and intermediate types could be distinguished by the morphology of the colonies and their cultural characteristics. After four to six weeks of growth on bouillon in aerobic conditions, intermediate types tended to change into mitis strains and this reaction could not be reversed even by passage through animals

The incidence of different types of diphtheria bacilli in Illinois has been studied recently by T C Grubb and H J Shaughnessy ⁵⁷ Among 162 strains isolated from 109 patients with diphtheria, only 5 5 per cent were found to be of the gravis type, 78 per cent intermediate, 29 per cent mitis and four per cent atypical In 20 per cent of the patients examined on several occasions, changes in type occurred from time to time In general, the intermediate types were recovered from mild, moderate and severe clinical cases and the gravis strains occurred in none of the severe or moderately severe clinical cases

The fact that severe diphtheria may arise from infection with mitis types of the micro-organism has led to the suggestion that the groups be classified as I, II, and III In a review of 73 patients with diphtheria, H Otto and G Mittag58 demonstrated the three types of infection, gravis, mitis and intermediate All three forms were observed during epidemics, and in healthy carriers Severe clinical diphtheria as well as dangerous complications occurred in patients with mitis types of micro-organisms and the authors believe that the above classification would be less likely to confuse the clinician in regard to the prognosis and general course of the disease.

Clinical Types and Complications

Two instances of primary diphtheria of the eye were observed recently by S. H McKee.⁵⁹ In two children, five and nine years of age respectively, conjunctivitis developed with a slight exudative membrane forming on the conjunctivae of the lids and palpebral borders. The diphtheria bacilli recovered from each case were proved to be virulent in type by animal inoculation. Diphtheria did not occur in other parts of the body of these patients

The diagnosis of cardiac complications of diphtheria has been aided considerably by electrocardiographic studies A recent survey of myocardial changes and disturbances of conduction occurring in diphtheria patients has been made by N. D Begg 60 Serial electrocardiograms were taken every one to three days in a group of 100 children with severe faucial diphtheria No abnormalities were noted in 16 per cent of the series, myocardial damage without conduction disturbances occurred in 57 per cent and severe lesions with conduction disturbances in the remaining 27 per cent Paroxysmal tachycardia, complete heart block, bundle branch block, intraventricular block were some of the most severe lesions which could be interpreted only by means of the electrocardiograms Diphtheritic carditis usually developed within three weeks after the onset of the initial disease

The permanency of postdiphtheritic cardiac lesions was investigated by A Beer 61. He examined 40 patients several years after their acute illness and found that four of the group had clinical evidence of mild cardiac involvement and that three had only inconsequential electrocardiographic changes. The remainder of the series were in good health so that the author concluded that children who survived the first few weeks of their diphtheritic carditis would probably make

steady and complete recoveries The possibility of diphtheria being a basis for many cardiac impairments of adult life seemed very remote

A re-examination of the hearts of a group of 100 patients who had suffered severely from diphtheria 15 to 20 years previously was conducted by W P Thompson, S E Golden and P D White 62 The histories of these patients indicated that all but four had been well during that period of time, two had suffered rheumatic attacks, one had developed hypertension with hemiplegia and one woman had a permanent hypertension following toxemia of pregnancy

One patient of the entire group had a heart of increased size due to combined mitral and aortic valvular lesions and six patients had premature contractions occurring rarely Murmurs heard in this group of patients were either functional (40 patients) or organic, resulting from intercurrent rheumatic fever infections. Blood pressures were normal except in the two patients with hyper-Electrocardiographic findings demonstrated auriculoventricular conduction rates at the upper limits of normal in three patients and possible intraventricular conduction disturbances in four cases. In the majority of the latter group of patients, the conduction times had become prolonged during the later years of the patients' lives, because the preliminary tests of 91 of the entire group ten years previously had not demonstrated this defect. There was the possibility that intercurrent rheumatic infection was the etiologic agent in these cardiac disturbances It was the conclusion of the authors that diphtheria may cause disturbances of conduction during acute stages of infection but that the scars of the disease very rarely account for such conditions in later life

Diphtheria bacilli so rarely invade the blood stream to cause foci of infection elsewhere that considerable interest is attached to the instance of endocarditis produced by this bacillus, observed by G J Buddingh and K Anderson 63 The patient had had a chronic epistaxis which required packing and apparently ulcerations had developed which allowed the diphtheria bacilli to enter the blood stream Vegetations developed on the mitral valve on the scars of a previous rheumatic infection From these vegetations, emboli spread to the heart muscle, kidneys, skin and mucous membranes The micro-organism was proved to belong to the diphtheria group by its morphology, cultural characteristics and by animal inoculations

Treatment — That diphtheria antitoxin is less effective in patients who are sensitive to serum has been maintained by some clinicians and denied by others. In experimental animals the rate of elimination or destruction of antitoxin is much greater in those that are sensitized than in normal ones. In order to investigate the problem from a climcal viewpoint, I. Davidsohn and L. W. Hunt⁶⁴ studied the therapeutic effects of antitoxin in groups of patients with various degrees of sensitivity course of the illness and complications of the disease were observed in 40 patients who developed reactions to the serum within 24 hours after its administration, in 164 patients with ordinary serum sickness and in 97 patients with as severe diphtheria but with no reactions to the serum. The results indicated that sensitivity to serum manifesting itself within the first 48 hours tended to diminish the effect of the antitoxin so that the severity of the illness and the number of complications of diphtheria were greater in the sensitive patients Delayed serum reactions did not seem to diminish the effectivity of the antitoxin. It was the conclusion of the authors that the production of passive immunity might be aided in persons showing immediate serum reactions by giving larger or additional doses, or by using antitoxin prepared from some other animal serum to which the patient was not sensitive

With increasing knowledge of vitamin C and its value in combating various infections, there has been some indication that it is needed by diphtheria patients H Otto⁶⁵ administered cevitamic acid to 42 patients with diphtheria in addition to the regular treatment and compared the course of the disease of this group with that of a similar group of 50 patients treated in the ordinary manner No differences were noted in the time required for the membrane to disappear, the number of complications or the mortality rate A difference did occur in the frequency of hemorrhages in the two groups, the ones receiving cevitamic acid having almost no sequelae of that sort The excretion of cevitamic acid was found to be very slight in diphtheria patients and the author was led to believe that the retention of this vitamin indicated the need of it by diphtheria patients, probably as a protection for the capillary blood vessels

The administration of sodium chloride seemed to be of value in the treatment of the diphtheritic patients observed by A MacLean 66 A teaspoonful of table salt was administered three times a day for three weeks to all patients except those with the most severe infections who were given intravenous injections of 30 cc of a five per cent saline solution. Patients were divided into four groups according to the severity of the disease and each one of these treated groups were compared with untreated patients having infec-

Those treated with extra amounts of salt seemed to have less severe manifestations of the illness. The author thought there might be some relationship between adrenal insufficiency and the demand for sodium chloride.

Immunization - Many clinical tests are being made to determine the comparative value and dosage of the various types of agents used to produce active immunization against diphtheria comparative study made by H C M Williams, J D Dear and W. Stewart⁶⁷ has shown that the single injection of alum precipitated toxoid is insufficient to produce the required immunity Of a group of 190 susceptible children under ten years of age, who received this form of treatment, about 15 per cent still had positive Schick reactions by the end of a year Employing other types of material, such as toxin-antitoxin, or toxin-antitoxin floccules, the number of Schick reactions changed from positive to negative in all but about one or two per cent of patients tested Although diphtheria occurred among patients who had received the immunization treatment, in none of these patients had a negative Schick test been obtained before the onset of the clinical disease

A single dose of alum toxoid administered to 63 children seemed effective in producing an immunity in the majority of patients who were retested 11 to 27 months later. The group, treated by H. W. Straus⁶⁵ were institution children, eight months to ten years of age. Each dose of toxoid contained 22 to 24 Lf doses and the reactions were negligible. Only 47 of the group received subsequent. Schick tests and 44 were found to be negative.

The necessity of employing at least two injections of alum toxoid to provide a more permanent immunity to diphtheria is emphasized by the report of H H Pansing and E R Shaffer ⁶⁹ Two groups of school children receiving a single dose of toxoid developed negative Schick reactions in 84 and 86 per cent of instances when tests were made one or two months after treatment. When a series of these negative reactors were retested two years later, 58 per cent were found to have slipped back into positive zones again. Children who received two injections of alum toxoid retained their immunity for a longer period of time.

For adults the problem of the best type of antigen to employ for immunization against diphtheria is even more difficult The experience in immunizing a large group of nurses over a period of 18 years has been reviewed by I V Cooke 70 In this series of more than 1000 young adults 63 per cent were found to be susceptible to diphtheria Various types of immunizing material were employed from time to time, including toxin-antitoxin, the ordinary toxoid material and the alum precipitated toxoid It was the conclusion of the author that, judging from the Schick test results and the incidence of diphtheria in this group, two injections of alum toxoid administered several months apart or three injections of plain toxoid given at intervals of several weeks between doses, proved to be the most effective methods of producing immunity The patients' reactions to the materials differed somewhat, the plain toxoid giving severe local reactions and systemic symptoms more frequently than the toxin-antitoxin, while the reactions from the alum precipitated toxoid were more numerous and severe than with either of the two other antigens, but it was the opinion of the author that in no instances was the discomfort of these methods so severe as to contraindicate

their use He stressed the point that the type of material obtained from one manufacturer might give more severe reactions and be much less suitable for the use in adults than the products of other concerns. During the period of observation, diphtheria of a clinical nature had been reduced in this group of nurses from about 29 per cent to 0.2 per cent. The duration of immunity was ascertained in several instances and among a group of 102 who were retested 6 to 16 years after immunization with toxin-antitoxin, 95 per cent were found to have retained their immunity

The results of immunization of young adults against diphtheria has also been reported by R E Boynton and R V Ellis 71 A group of 1900 university students, with positive Schick reactions, were injected with 0.5 cc of alum precipitated toxoid Severe reactions occurred in 34 of the group, and five of these developed sterile abscesses majority had some mild local reactions and only 21 per cent of the entire group had no reactions Preliminary tests for sensitivity of the patient to the proteins of the immunizing material (Moloney test) gave accurate information of the severity with which the patient would react to the injection of toxoid Some patients, however, with positive Moloney tests did not have reactions to the toxoid injections Retests of the group in two to four months after the moculation indicated that 89 per cent had been made Schick negative

In order to increase the amount of antitoxin in newly born infants and to prolong the duration of their passive immunity, M Magara⁷² advocated the administration of two doses of toxoid to mothers during their pregnancy. This treatment greatly increased the mothers' resistance to diphtheria and led to the transference of large amounts of anti-

toxin to their infants by way of the placenta. This procedure guaranteed immunity to the newborn for at least six months after their birth. Although the mothers tended to eliminate the antitoxin by various routes, including the breast milk secretion, for periods of six months or longer, they retained sufficient amounts of antitoxin to afford adequate protection for the next child, providing that it arrived within a year or two after the first one

A complication of unusual severity following the administration of diphtheria toxoid has been reported recently by S J Wilkinson 73 In a child one year of age, 05 cc of alum precipitated diphtheria toxoid was injected subcutane-Within the following week he developed weakness and finally paralysis of most of the muscles of the arms, legs and body The symptoms lasted for about two weeks and then the patient recovered slowly until about three months later he was completely well The condition was diagnosed as multiple neuritis and was thought to be due to the anaphylactic or allergic response of the patient to the injected material

The Schick Reaction - Failure of the Schick test to determine accurately the immunity of a patient has been given as the cause of many discrepancies of immunization results which have occurred in recent years. A comparative study of the reaction to various Schick testing materials has been conducted recently by K F Brandon and D T Fraser 74 Fifteen different commercial products were tested in a group of 87 persons, each patient receiving injections of six different products In 38 per cent of instances, the patients had positive reactions to all products, 28 per cent had negative responses to all products, but 34 per cent had inconsistent reactions

Of the total group, 26 per cent showed considerable disagreement in the type of reaction produced In testing the antitoxin content of the blood serum of patients who reacted positively to all of the Schick products, it was found that those having $\frac{1}{2}$ to $\frac{1}{2}$ or more of a unit of antitoxin had negative readings Those having less than 1/500 of a unit were generally positive with the exception of a small group in which the reaction could not be interpreted accurately The reactions of patients to six control materials also varied considerably The Schick control materials prepared by dilution methods were the types which gave more satisfactory results as far as the final determination of the immunity of the patient was concerned It was urged by the authors that standards of production of Schick testing toxins and of control material be more adequately established and followed

Allergic reactions to the Schick test have been described by A E Keller and S Harris ⁷⁵ Two young adults who had had Schick tests previously without unusual reactions received injections of alum toxoid and subsequent Schick tests Acute allergic responses followed the last skin test. The reactions, which consisted of urticaria, edema, and difficulties of respiration, required symptomatic treatment with adrenalin

Diphtheria Carriers—In order to be sure that a patient does not harbor diphtheria bacilli, repeated cultures of the nose and throat have been advocated by E. Lenz 76. By taking cultures from the nasopharynx at two hour intervals from 6.00 a. M. to 8.00 p. M., she found that 30 per cent of a group of carriers would not have been detected by a single culture only. Positive results could be obtained most readily from swabs taken in the early morning hours.

ENDOCRINE DISTURBANCES

By Josef Warkany, M D

Pituitary

Review-A review of articles on the hypophyseal-diencephalic system been made by W Raab 77 In his opinion the results of experimental, clinical and anatomical studies indicate that the hypophysis and the diencephalon are in close relationship not only embryologically but also functionally Hypophyseal hormones travel into the diencephalon and there with the help of nerve tracts become effective on far distant organs and systems of organs On the other hand, the secretory activity of the hypophysis is regulated from the diencephalon, partly with the help of hormones, carried by the blood stream and derived from glands that are considered to be subordinate to the hypophysis By this mechanism these glands exert a certain control over the hypophysis Moreover the nervous tissue of the floor of the diencephalon seems to have the ability to produce hormone-like substances, which can, if necessary, make up for a deficiency of the hypophysis Pituitary hormones are also found in the hypothalamus or in the cerebrospinal fluid It has also been proved that the hormones of the posterior pituitary exert their effect through the diencephalon Since some of the pituitary fractions have also been found in the blood stream, it is possible that the hormones are discharged in two directions (1) Into the spinal fluid and the hypothalamic substance, and (2) into the blood stream From a clinico-pathogenetic standpoint, the majority of the so-called symptoms of pituitary deficiency can be explained either by primary pituitary or primary diencephalic disturbances or by a combination of the two The type of treatment can best be determined by a pathogenetic analysis of each case Great

difficulty is often encountered, because the diencephalic centers have lost the power to react to hormonal stimuli. Substitution therapy is then impossible

Growth and Growth Disturbances -Differential cell counts of the pituitary in thymus-treated strains of rats have been performed by J H Clark, A Steinberg and L G Rowntree 78 The authors, in an attempt to ascertain the possible mechanism of the previously reported acceleration in the rate of growth and development of rats produced by injections of thymus extract, have made differential cell counts of the pituitaries in a series of rats at intervals between birth and 45 days of age, the period of most rapid growth It was found that the percentage of acidophils seemed definitely higher in the thymus-treated, precocious strain between birth and about 15 days of The correlation between rapid growth in thymus-treated animals and acidophil content of the pituitary seems to be substantiated, by these experiments The body weight bears a definite relationship to the acidophil count in the pituitary in both control and thymustreated rats

The second and final report of the study of a group of six dwaifish children who have been under observation for nearly five years has been made by E K Shelton, L A Cavanaugh and H M Evans 79 Five of the patients were given alkaline extract of the anterior lobe of the hypophysis intramuscularly. One never received such treatment. One child died as a result of a recurrent cyst of the suprasellar pouch. Stimulation of growth was actual in one patient and apparent in two. One control patient grew rapidly in the second period of observation although no treatment was given.

one minor physiologic accident was observed. Development of refractoriness in the treated children was not apparent The authors point out the difficulties and vagaries of such a clinical research It appears to them that the title "Hypophyseal infantilism" was probably ill chosen While it still seems likely that at least three of the subjects were suffering from arrested growth as a result of the pituitary embarrassment, the authors are almost equally certain that two of the subjects were not They come to the following conclusions The anterior pituitary extract employed in the study will promote growth in the human subject when administered intramuscularly The stimulation of growth appears to be in direct ratio to the amount of the extract administered From a purely clinical standpoint, the growth promoting property is disappointing. The preparations are not sufficiently active to rehabilitate the classic dwarf. The preparations may be clinically useful in the rehabilitation during the growing period of dwarf-1sh persons who are losing not over 50 per cent of the normal growth incre-Prolonged administration produces little evidence of a subsequent refractory stage and does not interfere with either the onset of puberty or the spurt of growth which may occur in this period Prolonged and intensive administration is not without an element of physiologic danger

Successful treatment of infantilism with anterior pituitary extract is reported by M M Goldberg 80 Coincident with the administration of 37 5 cc of an anterior pituitary extract over a period of approximately 4½ months, a male patient exhibiting the cardinal symptoms of pituitary infantilism of the Levi-Lorraine type grew two inches in height and exhibited definite stimulation of the primary and secondary sexual character-

istics Growth continued after the cessation of treatment and was approximately $1\frac{1}{8}$ inches (2.5 cm.) in four months During the period of treatment the boy gained 6 pounds (27 kg.), and subsequently $4\frac{1}{2}$ pounds (2 kg.).

A hypothesis that renal rickets and dwarfism is a pituitary disease has been advanced by B Chown and M Lee 81 Their patient, a girl, aged 181/2 years, had been apparently normal as an infant but was slow in learning to talk and walk At the age of two years, she had an acute illness at a time when encephalitis was epidemic in the community Her urine was normal Soon there developed polyuria and polydypsia of such intensity that she drank from the toilet The authors feel safe in saving that these symptoms could not have been due to chronic nephritis, for 15 years later the urea nitrogen content of her blood was only 30 to 45 mg per 100 cc and the clearance of the urea from 28 to 37 per cent The authors think that the polyuria at the onset could be explained as simple diabetes insipidus, as evidence of abnormal traffic in some unknown metabolite requiring large quantities of water for its excretion, or as evidence of parathy-101d overactivity. At the age of eight years numerous pus cells were repeatedly found in the urine The authors present experimental evidence to show that pyuria can result from mineral deposits in the kidney and it is possible that at the onset of polyuria in these patients a comparable mineral assault is taking place If such is the case, destruction of the kidneys might gradually progress, the primary pyuria might merge with secondary pyuria due to renal failure. It is of interest to note that the patient did not react to injections of posterior pituitary

At the age of 16, after the onset of delayed prepubertal growth, the zone of metaphysio-epiphyseal junction became

soft, allowing the deformities to take place The function of the kidneys was low at that time, the excretion of calcium reduced and the excretion of phosphorus normal On the other hand the blood calcium and phopshorus levels were normal at rest, although they were labile as in rickets or parathyroprivia Histologically the shaft of the femur was porotic This could scarcely be the result of disuse since the patient had been up and about until the day of the first operation At the time of the final examination, the patient was a dwarf with reduced kidney function, pyuria, ricketslike changes in the long bones and delayed sexual development She had a high, normal vitamin D content of the blood and her bone lesions did not respond to the administration of vitamin She, therefore, was not suffering from avitaminotic rickets Her blood calcium level was never found to be high Her urinary phosphorus was not found to be increased and the shafts of her femurs did not show any increase in osteoclastic activities

These facts, according to the authors, ruled out a diagnosis of primary or secondary hyperparathyroidism, while chemical studies showed that there was not a continuous process of active destruction of the kidneys through increased mineral excretion The authors are attempting to find a factor which will cause the following symptoms (1) Polyuria, (2) dwarfing, (3) infantilism, (4) lability of the blood calcium and phosphorus level, (5) destruction of the kidneys, and (6) faulty growth of the bones They think that disease of the diencephalopituitary region could produce the first three symptoms and they discuss the hypothetical possibility that the last three symptoms could also be caused by the same pathologic process.

D. L Sexton and F Neuhoff⁸² have reported the case of a girl of 25 years with diabetes of late onset and a classic picture of pituitary infantilism (dwarfism) The case was paradoxical in that hypopituitarism is commonly associated with augmented sugar tolerance case can not be primarily one of diabetic infantilism because the patient was 19 years of age before glycosuria was dis-Infantile statural and sexual development without demonstrable organic cause plus the finding of delayed union of the epiphyseal centers constitute the cardinal signs of pituitary However, diabetes in this dwarfism case is believed to be of true pancreatic origin It was due to the deficiency of insulin and its occurrence is considered to be entirely independent of the pituitary syndrome

The clinical and laboratory findings and the result of treatment of endocrine obesity in 50 children, 29 boys and 21 girls, have been reported by M Gordon 83 He thinks that overeating per se is an infrequent cause of obesity The endocrine factors are ın children disturbances of the thyroid, pituitary, adrenal and sex glands A table for differential diagnosis between the thyroid and pituitary types of obesity is offered The etiologic types represented in the series are (1) Hypopituitary (86 per cent), (2) hypothyroid (12 per cent), (3) hypogonad (two per These figures indicate that the cent) pituitary obesity with or without secondary hypothyroidism is much more frequent than the primary hypothyroid or the primary hypogonad type in child-The average initial overweight in this series was 44.4 per cent on the basis of height and age as compared with the Baldwin standard, ranging from 9 to 143 per cent overweight The majority of children were of average normal height for the age or taller, only five were below average height for age The sexual development was normal in two boys and retarded in 27 Cryptorchidism was present in five unilaterally and seven bilaterally disturbances were present in nine girls of postpubertal age, including one with primary eunuchoidism. On the basis of actual weight a basal metabolic rate below - 10 was noted in 55 per cent of the children, between + 10 and - 10 in 41 per cent and above + 10 in four per cent The specific dynamic action is diminished in childhood endocrine obesity

Blood chemistry studies indicate that endocrine obesity is combined with high values of chloride, uric acid and high normal content of cholesterol, low normal values of sugar and normal content of urea nitrogen and creatinine and water retention are present in the majority of cases The treatment in this series consisted of, first, low caloric diet, high protein, low fat and carbohydrate and restriction of salt and water intake, second, oral administration of desiccated thyroid and anterior pituitary gland substances and third, hypodermic injection of anterior pituitary extract and hypoderinic injection of extract of pregnancy urine or of female sex hormones in cryptorchidism and menstrual disorders and protracted cases of hypogonadism

Practically one-half of the number of children treated were reduced in weight to normal or to within ten per cent overweight for height and age on the basis of accrued height. There was a redistribution of fat toward a more normal allocation and a general increase in height in spite of the low caloric diet. There was an average increase of 8.5 in the basal metabolic rate for the period and an increase in specific dynamic action. This apparently was more marked

in the lower than in the upper levels. Hypogonadism and cryptorchidism were benefited to a greater extent than were menstrual disturbances in girls. The degree of improvement in the component parts of the external genitals was not uniform. Untoward results noted during treatment consisted of urticaria, angioneurotic edema, pleuritis, abdominal colic and loose bowel movement; acute congestion of the testes was noted in two instances of hypogonadism followering the use of anterior pituitary-like extract.

G B Dorff⁸⁴ has described the treatment of nine patients ranging in age from 3 to 14 years with undescended, hypoplastic testes and with hypoplastic external genitalia Eight of these patients were of the adiposogenital dystrophic type The author has classified them in order to indicate what he believes is the primary offending gland causing the insufficiency, such as the thyroid, the gonad or the pituitary The cases in this series reported were only of the hypothyroid and the hypogonadal types and did not include any of the hypopituitary type The treatment varied from the gonadotropic hormone of pregnancy urine with dietary restriction in the hypogonad patient and the gonadotropic hormone of pregnancy urine, dietary restrictions and the supplementary use of dessicated thyroid in the hypothyroid patient Unusual complications, such as torsion, mechanical obstruction and hernia, are briefly discussed The question of whether the descent of the testes was mechanical or hormonal is considered According to the author, value of combined therapy was shown in that not only was genital development stimulated and genital maldevelopment corrected, but also many of the other accompanying deficiencies of a skeletal, somatic or mental nature could usually be improved and redirected towards the normal

Two cases of obesity in children due to overeating have been observed by L Frey 85 He thinks that obesity in children on a purely endocrine basis is a rare condition In most cases, according to the author, obesity is due to habitual overeating He illustrates his point by reports of two cases In both cases good results were obtained by a low caloric diet without any glandular treatment In the second case, however, the author admits that an endocrine factor could not be excluded This case concerns a boy, three years old, who was 578 pounds (263 kilograms) overweight He was also 4 inches (10 cm) too tall This child was treated by a diet of 400 calories per day On this diet he lost about 66 pounds (3 kilograms) every month and after seven months he had lost 48 4 pounds (22 kilograms) and had become 08 inch (2 cm) taller This remarkable effect of a reduction diet 15 illustrated by photographs

The usefulness of the oral administration of pituitary extract has been emphasized in a report of two cases of adiposogenital dystrophy by L. A. Lurie 86. His patients were treated by the oral administration of extract of pituitary gland without resorting to drastic limitations of caloric and fluid intake. Both boys lost in weight. Their desire for food, especially for carbohydrate and water returned to normal. Their headaches disappeared Pubertal changes were brought about. Their sluggishness and general phlegmatic attitude disappeared and they became mentally more alert.

A behavior study in cases of *Froelich's* syndrome has been made by D M Levy ⁸⁷ The author believes that the submissive behavior in these cases is due to a constitutional factor. It can not be explained by the early life history, by a

psychologic response to the obesity or the hypogenitalism or by the maternal attitude. Aggressive and submissive tendencies are presumably based on instinctive responses in social life. The strength of these responses is determined both by constitutional and by experiencial factors. On the basis of this study the author concludes in general that even though it is constitutionally determined, a trend may be magnified or diminished by the life experience.

The results of transplanting calves' pituitaries in Simmond's disease (23 cases) and in adiposogenital dystrophy (one case) have been reported by E Kylın 88 A young man, 19 years of age, who suffered from adiposogenital dystrophy was cured completely five months The testes were enafter operation larged, the distribution of fat and hair was readjusted and the patient appeared like a normal man Of 23 patients with Simmond's disease complete cure was obtained in 12 patients. Their body weight increased, in one case by 30 kilograms In six cases a definite improvement could be noted. Since in some of the patients the time of observation was too short, the final results cannot be reported yet Two patients died without showing improvement, one immediately and one three months after operation Although children are not included in Kylin's series, his results are of such interest that they deserve to be abstracted here

A case of *obesity*, polydactylism and syndactylism, mental retardation and retinitis pigmentosa (Laurence-Moon-Biedl syndrome) has been described in a white girl, seven years old, by J M Arena ⁸⁹ The case is especially interesting because one brother of the patient died at the age of 18 years of congenital heart disease

A case of multiple defects (polydactylism, deformed legs, mental retardation,

obesity) has been described by A G Levingston ⁹⁰ The eyes were normal Hypogenitalism was not evident at the age of 13 The author considered this case as showing about 70 per cent of the signs and characters belonging to the symptom-complex classified as the Laurence-Moon-Biedl syndrome

I Warkany, G S Frauenberger and A G Mitchell⁹¹ have reviewed the literature of the Laurence-Moon-Biedl syndrome and reported two incomplete cases. They come to the conclusion that the Laurence-Moon-Biedl syndrome is not an unalterable unit but a more or less frequent combination of certain developmental abnormalities (obesity, hypogenitalism, retinitis pigmentosa, polydactylism and mental deficiency) The syndrome is often found to be incomplete and sometimes it is observed in combination with other developmental defects, like congenital heart disease, epicanthic folds, dwarfism, etc

G B Dorff and L M Shapiro⁹² have made a clinical-pathologic study of cases of sexual precocity with hydrocephalus The cases of two young girls showing a similarity of symptoms such as chronic internal hydrocephalus, spastic paralysis and macrogenitosomia praecox without menstruation are reported One of these cases was studied at necropsy. In addition to the existing hydrocephalus, pathologic studies of the ductless glands showed a normal pineal gland, one normal parathyroid gland, inconsequential involvement of the thyroid and adrenal glands, an enlarged, somewhat compressed pituitary gland and many follicular cysts in the ovaries The follicles were in various stages of maturation but none exhibited luteinization. It is suggested that the chronic increased, intracranial pressure with compression of the hypothalamic-infundibular-hypophyseal pathway was the starting point for the development of the precocious state Several cases of examples of pubertas praecox and macrogenitosomia praecox in males and females (with and without menstruation in the females) without any apparent lesions in the endocrine glands which one usually associates with precocity are reported from the literature.

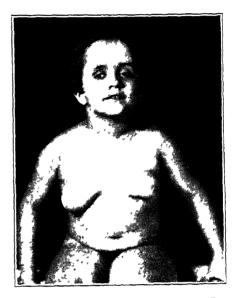


Fig 1 (case 2)—Photograph of A D at 6½ years of age, showing the enlargement of the head, well-developed breasts and pubic hair (Courtesy, Amer J Diseases of Children)

Water Metabolism-E Wentzler observed a case of cancer of the pituitary in a boy, aged nine years A boy, $8\frac{1}{2}$ vears old, was admitted to the hospital on account of extreme emaciation and the symptoms of diabetes insipidus, polydypsia and polyuria. The diabetes insipidus did not respond to injection of posterior pituitary extract. There seemed to be some favorable influence of insulin treatment on the child's body weight At the age of nine years, the child died The necropsy showed the following findings Carcinoma of the hypophysis with complete destruction of the posterior lobe and tuber cinereum. The anterior lobe was not affected at all

Two cases of polycythemia combined with diencephalic-hypophyseal lesions have been described by N W. Barker and W. M Craig 94 These cases could not be classified as polycythemia vera because of the normal blood volumes and the absence of splenomegaly authors discuss the possibility that the cerebral lesions were secondary to preexisting polycythemia They also quote Cushing's belief that the posterior lobe and the stalk of the hypophysis of the hypothalmic region are all concerned in water metabolism In all the previously reported cases, as well as in the cases reported by the authors, there was clinical or pathological evidence of lesions involving one or more of these parts of the brain Therefore, it has seemed logical to the authors to suspect that relative polycythemia, in other words, concentrated blood with low plasma volume may be produced by a lesion of the brain centers controlling water metabolism

In six patients with polycythemia vera the urinary excretion of gonadotropic substance has been studied by S. L. Israel and T H Mendell⁹⁵ in an attempt to evaluate the currently discussed relationship of the disease to the hypophysis No significant data have been uncovered by this investigation masmuch as none of the six patients showed a demonstrable excessive quantity of hormone in the urine The absence of urinary gonadotropic principle in patients with polycythemia vera has, however, no bearing on the possible etiologic relationship of the water metabolism center to this disease

D Wilson⁹⁶ has investigated the effect of anterior pituitary-like hormones on the blood picture in rabbits. Injections of anterior pituitary-like hormone extracts such an Antuitin-S caused a marked leukocytosis in normal virgin female rabbits within five to eight hours

after the injection The red cell count remained unaltered Repeated injections over a long period and at short intervals became ineffectual in producing a leukocytosis

Thyroid

Metabolic Studies-The level of the intake of calcium on the blood iodine has been investigated by J Thompson 97 Five hundred and forty rats on specific synthetic diets in which there was a variation in the calcium-iodine ratio were studied over a period of seven months The results of chemical analysis have shown that the amount of calcium in the diet influences the level of iodine in the blood In animals on diets containing the same amount of iodine, the blood iodine level was comparatively lower in the groups receiving additional calcium than in the controls On high iodine diets there did not appear to be any close relation between the amount of iodine consumed and the level of the blood rodine In contrast the average serum calcium level was not markedly affected by varying the dietary iodine

When the calcium-iodine ratio of the diet was altered beyond certain limits, different clinical manifestations peculiar to certain experimental groups devel-The rats on low 10dine diets showed many of the clinical changes found in human cases of exophthalmic Animals maintained on a diet low in calcium and high in iodine developed signs resembling iodism. The experimental findings relative to iodism were considered to indicate that iodine induces the syndrome only under spe-The concentration of cial conditions iodine in the blood is not the determining The intake of calcium has an important influence in that an excess in the diet acts as a prophylactic whereas a deficiency favors the development of iodism.

E P and D. R. McCullagh⁹⁸ reported their clinical experiences in use of determinations of blood iodine They found (in Cleveland) that blood iodine levels of normal adults and of patients who had diseases which are not associated with the thyroid glands ranged from approximately 8 to 12 micrograms per 100 cc The blood iodine level was very high in cases in which iodine medication had been instituted. Exercise had little influence in raising this level Under controlled conditions it was proportionate in most cases to thyroid activity, the change in the level being relatively greater in persons with hyperthyroidism than in those with hypothyroidism hyperthyroidism values between 11 1 and 498 micrograms per 100 cc were found, while in hypothyroidism the values ranged between 63 and 108 micrograms per 100 cc. The authors conclude that these determinations of blood iodine are of value in the differential diagnosis of hyperthyroidism

C H Boissevain and W F Drea99 have examined the relation between the occurrence of endemic goiter and the presence of traces of silver and barium in drinking water. It is generally admitted that iodine deficiency is a primary cause of endemic goiter. Any factor that interferes with the utilization by the organism of the iodine present may constitute a secondary cause. According to many investigators infections and contamination of the water supply are such factors The presence of chemicals that interfere with the assimilation of iodine by rendering it insoluble may well be another contributing cause of goiter During a spectroscopic examination of the water supply of Colorado, the authors noticed that strong traces of silver are present in the drinking water in regions where goiter is endemic thought that minute traces of silver can

make a large part of the iodine insoluble and thus render it unavailable for the organism. In a spectrographic examination of drinking water from both goitrous and nongoitrous regions, traces of silver were found. Water from the Swiss goiter region showed an unusually large amount of barium. Feeding experiments, using rats as experimental animals, failed to show any influence of either silver or barium on the development of goiter

Creatine studies in thyroid disorders were made by G W Thorn 100 The creatine tolerance test as described by Richardson and Shorr was employed with slight modification in a study of 12 patients with thyroid toxicosis, and in seven patients with well developed, typical spontaneous myxedema A marked impairment in the retention of creatine in the patients with thyrotoxicosis was noted in all instances Iodine reduced the creatinuria and improved the creatine retention in thyrotoxicosis. Proof of a primary effect of iodine upon creatine metabolism was lacking The alteration in creatine metabolism may persist for many months following the subtotal thyroidectomy performed for the relief of In patients with the thyrotoxicosis myxedema creatinuria often preceded the metabolic rise following thyroid admin-The creatine retention decreased in myxedematous patients under thyroid therapy.

Basal metabolic standards of girls have been presented by F B Talbot, Edwin B Wilson and Jane Worcester ¹⁰¹ According to the authors, the standard of metabolism used for adults has worked out satisfactorily. There is a difference, however, with the study of metabolism during childhood, which is a period of constant change and development. The standards are fairly complete for persons of both sexes up to puberty, but few normal persons have been studied care

fully from puberty to the age of 20 years Some of the gaps have been filled in by various workers but blank spots which need more study remain this in view, the authors have obtained the metabolism of 106 healthy normal girls attending a private school in Bos-This study of physiologic background and application of standards is summed up by the authors in the following way "Before generalizing, we must draw attention to certain factors which we believe modify the metabolism They include geographic situation, which cannot be separated from climate Knowledge to date indicates that the level of the metabolism is different in different latitudes If the standards presented here are generally accepted, a correction should be made for the locality in which the investigator works. We do not believe that race affects the metabolism

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"There is a very definite relation between body weight and heat production Mathematically, the correlation of heat production is closer with body weight than with any other factor studied by us It has been shown by Brody, Procter and Ashworth that there is a similar close correlation between weight and the creatinine output not only in man but also in warm-blooded animals of all sizes nally, attention has been drawn to the correlation between the creatinine output and the basal heat production Since the creatinine output is accepted as a measure of active protoplasmic tissue, it may be said with assurance that the active protoplasmic tissue of the body is the principal factor of importance connected with heat production.

"Many accessory factors may modify the amount of heat produced even under basal conditions They are so interrelated that it is difficult to separate one effect from another Age, for example, seems to have some effect, and different eras

of life are physiologically unlike After birth there is tremendous proportionate growth in both height and weight, it reappears with a spurt at or about puberty, accompanied by other changes After this growth gradually diminishes and finally disappears entirely, when full growth is attained, the person enters adult life This may be earlier in some persons and later in others Growth usually terminates at about 20 years For the next two or three decades there are few changes in the normal physiologic processes Then comes the slow degeneration of old age, the onset of which varies with different persons

"The main difference between the adult and the child is that the former is a finished product which remains in the status quo and the latter is continuously changing. We have presented here considerable evidence to the effect that there is a relation between the speed of growth and surplus metabolism. This should be considered every time metabolism is interpreted by the clinician. Our evidence indicates that the elevation in metabolism seen just before puberty is not due to puberty per se but to the speed of growth

"The standards presented here are, like all other standards, averages If they are used, the coefficient of variability should always be kept in mind. They have the advantage of being direct measurements which require no formulas and are thus open to less possibility of accumulation of errors. They include new data which help to fill in the blank spaces of from 12 to 20 years and thus connect young childhood with adult life."

The basal metabolism of normal boys and girls from two to 12 years old, inclusive, has been investigated by Robert C Lewis, Gladys M Kinsman and Alberta Iliff 102 The results of studies conducted during the past four years as a part of the general program of the Child Re-

search Council with data sufficient for interpretation within the age groups of from two to 12 years have been presented. The summary and conclusion of this article follow.

"As a report of progress in a longitudinal study of normal children, the results of 366 basal metabolism tests on 52 boys and of 271 basal metabolism tests on 41 girls, all between the ages of two and 12 years, inclusive, are presented The tests were made by means of the open circuit chamber method and the Carpenter-Haldane gas analysis apparatus

"The results are presented in a cross-sectional manner, and the heat production is expressed as calories per hour referred to age, weight, height and surface area, respectively, and as calories per hour per square meter of surface area, calories per hour per kilogram of body weight and calories per hour per centimeter of total height, respectively, referred to age

"The means, the standard deviations from the means and the coefficients of variation of the observed heat production for convenient arbitrary divisions of the variable to which the heat production was referred were computed for each of the specific methods of expressing the energy metabolism

"The mean coefficient of variation, a statistic which was used to indicate the degree of scatter of the individual tests, was found to be of increasing value in the following order

Boys

1 and 2 Calories per hour referred to surface area

and

Calories per hour per square meter referred to age

- 3 Calories per hour referred to weight
- 4 Calories per hour referred to height
- 5 Calories per hour per centimeter referred to age

6 and 7 Calories per hour referred to age and

Calories per hour per kilogram referred to age

Girls

- 1 Calories per hour referred to weight
- 2 Calories per hour per square meter referred to age
- 3 Calories per hour referred to surface area
- 4 Calories per hour per centimeter referred to age
- 5 Calories per hour referred to height
- 6 Calories per hour referred to age
- 7 Calories per hour per kilogram referred to age

"This treatment of the data indicates that for the group of normal children under investigation three of the methods of expressing heat production, calories per hour referred to weight and surface area, respectively, and calories per hour per square meter referred to age, give the lowest degrees of dispersion

"The mean coefficients of variation for these three methods show that theoretically 99.7 per cent (the percentage included within plus and minus three standard deviations from the mean) of all the test should fall within \pm 18 per cent of the mean for the boys and within \pm 16 per cent for the girls and that 95 per cent (the percentage included within plus and minus two standard deviations) should fall within \pm 12 per cent for the boys and within \pm 11 per cent for the girls

"Scatter diagrams for these three methods and for calories per hour referred to height were constructed, and in each case the central trend line was fitted either by the semi-average method or by inspection

"The central trend line values for calories per hour per square meter referred to age and for calories per hour referred to weight and to body surface, respectively, were tabulated in order that

they might be available as prediction standards.

"Even though they show somewhat greater dispersion than is the case with the three methods just mentioned, the central trend line values for calories per hour referred to height were also tabulated, since this method of expressing the heat production has found rather wide use in the literature.

"The relationship of the results of the present study to those reported by other workers was studied in detail by comparing the separate tests reported in the literature with the four central trend line values mentioned. Histograms of the percentage deviations were constructed. In cases in which the separate tests were not reported, the trends and levels of the results are shown graphically. The comparative results are discussed in detail.

"This analysis of the results of basal metabolism tests on children reported in the literature demonstrates the significant effects of body build on the comparative values obtained for the basal metabolic rate by the several methods of reference. The importance of considering the relationship between the body measurements of the children for whom the standards are to be used and the homologous measurements of the children with whom they were established is emphasized thereby.

"The precise relationship of body build to the basal metabolism of children cannot be determined until a more complete statistical study in close correlation with anthropometric and other physiologic measurements is made. Such an analysis will be warranted only when a larger collection of data is available.

"Since the Child Research Council project is a longitudinal study designed to extend over a period of many years, additional data on the basal metabolism of children are constantly being accu-

mulated, and further reports for the age groups represented in the present paper and for older and younger children may be expected in the future.

"In one of a series of studies on 'Growth and Basal Metabolism,' I. Nakagawa¹⁰³ has reported changes in the basal metabolism of children during puberty.

"The basal metabolism, together with the body weight and height, of 24 children, 10 boys and 14 girls, was studied every six months throughout the pubertal period.

"At puberty, there is a higher increase in the total heat production (at its maximum it amounts to above 100 calories a year) as well as in weight and height. This increase begins at the age of 11 or 12 years in boys and of 10 or 11 years in girls, which is consistent with the fact that girls attain puberty earlier than boys do; it reaches its maximum at the age of 12 or 13 years in boys and of 11 or 12 years in girls, and it ends, before the increase in weight and height does, at the age of 15 or 16 years in boys and of 14 or 15 years in girls.

"I calculated the coefficients of correlation between the total heat production and the weight, height, surface area and sitting height by using 131 sets of data obtained in the present experiment. Which physical factor is the best for expressing the amount of the heat produced has not been ascertained; nevertheless, in the individual children the weight was most closely correlated with the total heat production.

"The increase in the metabolic rate or the irregularity in its decrease per unit of weight or surface area may be due to the fact that total heat production increases greatly at puberty and that this increase reaches its maximum earlier than does the increase in weight or height. "Though the age at which this increase in the basal metabolic rate or an irregularity in its decrease reaches the maximum varies with individual children, the average is 14 for boys and 13 for girls, which is consistent with the earlier pubescence of girls. That is, the maximum is reached before the sexual maturity is established in boys and catamenia in girls. There seemed to be no uniformity in the height of the increased metabolic rate or in its duration, it varied with individual children.

"The increase in the total heat production probably occurs in preparation for the physical changes which take place at puberty"

Hypothyroidism

Late results of treated hypothyroidism in two children have been reported by L M Bayer and A W Snoke 104 These children were followed under treatment from the approximate ages of four to 18 years, and two to 11 years At first both children had the appearance, build and characteristics of thyroid deficiency and a significant retardation in height, bony development and mental development In both cases the complete restitution of osseous development was striking One girl developed a nicely proportioned body with quite a delicate face but remained permanently dwarfed Her intellect did not develop beyond the level of a child of 101/2 years. The younger one, on the other hand, retained her thickset build but compensated completely in height and mentality

The possibility of spontaneous remission in congenital hypothyroidism has been pointed out by J Siegl ¹⁰⁵ A patient with typical hypothyroidism was admitted to the hospital at the age of four months Without specific treatment the child showed improvement within a few weeks He became more lively,

learned to fix objects and to laugh. The symptoms of hypothyroidism slowly disappeared and a marked constipation which had been present improved. The child was discharged after a stay in the hospital of 12 weeks and was seen again at the age of $2\frac{1}{2}$ years. He then showed all the signs of severe hypothyroidism and thyroid treatment was again instituted. The author believes temporary spontaneous remission took place in this case of congenital hypothyroidism

Glycogen disease manifesting itself as a myxedema has been described by W Hertz and E Jeckeln ¹⁰⁶ The authors point out that children showing glycogen disease often present symptoms which can be considered hypophyseal-mesencephalic disturbances, although pathologic-anatomic changes of the hypophysis and the mesencephalon have not been demonstrated. They describe a case of glycogen disease in a child which appeared clinically as a myxedema (hypothyroidism). The thyroid gland was found to be present at necropsy.

The relation of thyroid and parathyroid glands to chronic arthritis has been considered by H J Viersma¹⁰⁷ who found the syndrome of an arthritic condition in certain cases of hypothyroid-1sm The shoulder joints were most often affected There was a high grade muscular atrophy and marked pains radiating to the arms. The symptoms subsided after subtotal thyroidectomy. In a case in which thyroidectomy was not performed, a progressive ankylotic polyarthritis with contractures ensued The authors also state that arthritis deformans is sometimes found in hypothyroidism In these cases thyroid treatment is said to be of value importance of the parathyroid gland in the etiology of chronic rheumatoid arthritis and spondylarthritis ankylopoietica is denied

Hyperthyroidism

G. Crile, Jr., and J L Blanton¹⁰⁸ have reviewed the literature on *exophthalmic goiter* in young children and have reported a case in a boy, 2½ years of age Thyroidectomy was successful in this case According to the authors this is the youngest patient to be operated upon successfully Seven other cases of unquestionable hyperthyroidism in children under five years of age have been reported in American literature

The relationship of the thyroid and parathyroid glands to calcium and phosphorus metabolism has been discussed by O Cope and G A Donaldson 109 They have studied a case with co-existent hypoparathyroidism and hyperthyroidism The patient described suffered from recurrent thyrotoxicosis and postoperative parathyroid tetany When the metabolic rate was maintained within normal limits by rodine medication, the calcium and phosphorus metabolic balance was chaiacteristic of parathyroid tetany During hyperthyroidism a marked increase in the negative balance of calcium and phosphorus beyond normal limits was found, even though signs of diminished parathyroid activity continued Increased thytold activity was followed by a rise in the subnormal blood serum calcium level toward normal and a decrease in the signs of tetany. The reverse occurred with a decrease in thyroid function. An acute upper respiratory infection was associated with an increase in the amount of clinical tetany and also with a spontaneous remission of the thyrotoxicosis Support is given to the belief that the change in calcium metabolism previously reported in hyperthyroidism is not due to a concomitant overactivity of the parathyroid glands The relation of the parathyroid and anterior pituitary and adrenal cortical glands in calcium metabolism is discussed

G Litzka¹¹⁰ has reported the usefulness of *fluorotyrosine treatment* in cases of *hyperthyroidosis* and *Graves' disease* This was proved by the change of the Reid-Hunt reaction and by improvement of the carbohydrate metabolism which is pathologically changed in these conditions

The history of the Reid-Hunt acetonitrile test has been surveyed by R F Escamilla 111 His efforts to repeat some of the work with a view to clinical application were unsuccessful because of the apparent impossibility of finding a sharp minimal lethal dose of acetonitrile in white mice A toxicity curve was constructed for the effect of acetonitrile on white mice and 12 Reid-Hunt tests were then attempted Eleven were negative and one positive The patient whose blood caused a positive test had a basal metabolic rate of +29 per cent, while among the negatives were very toxic patients with rates between + 643 and + 869 per cent As a result of this work the Reid-Hunt acetonitrile reaction is not recommended as an aid in the diagnosis of thyroid function

Relationship of the Thyroid to Miscellaneous Conditions

Studies in endocrine therapy in chilepsy have been undertaken by C Stein 112 Endocrine therapy chiefly with thyroid extract and dessicated whole pituitary bodies was given to 12 epileptic patients Eight of these patients showed a slight to moderate decrease, while four showed an increase in the number of their seizures during treatment Shortening of the post-convulsive period of debility was observed in five of the cases and in four cases there was a tendency to a prolongation of the aura General improvement in the health, metabolism. pulse, weight, blood pressure and bowel habits was noted in the majority of the cases The results of these studies indicate that in selected cases of epilepsy, thyroid medication, carefully controlled, is of some value in improving the general health of the patient and thereby raising the convulsive threshold

An investigation on the pathogenesis and treatment of myotonia congenita has been conducted by H G Poncher and H Woodward 113 A prolonged study of the creatine creatinine metabolism of an infant with myotonia congenita (Thomsen's disease) revealed the following features The physiologic creatinuria of infancy and childhood was absent, although the patient was ingesting an adequate amount of protein Creatinuria appeared on the administration of thyroid and the amount of creatine excreted appeared to have a relation to the size of the dose of thyroid The excretion of the creatinine was not significantly affected by the administration of thyroid A carefully controlled dosage of thyroid rendered the patient symptom-free The administration of 1 Gm of creatine by mouth while the patient was symptomfree caused the return of the myotoma, although an approximately normal proportion of the ingested creatine was ex-A decrease in the amount of creatine excreted was invariably associated with myotonia Either condition might appear first in spite of the fact that the patient was receiving thyroid injections Whooping cough and measles caused a decrease in the amount of creatine excreted and the return of the myotonia An increase in the dose of thyroid relieved the myotonic symptoms even in the presence of infection The amount of creatine excretion remained small during the persistence of the infectious conditions in spite of an elevation of temperature

Thyroid dysfunction in hemochromatosis has been studied by M N Orgel

and D P Barr ¹¹⁴ In hemochromatosis the functional activity of the thyroid may depend on the response produced by the deposit of iron pigment. The case presented here and other cases in the literature suggest that at first the pigment increases the thyroid activities, but as pigment deposition increases and fibrosis sets in there is a progressive decrease in function. Examination of 101 thyroid glands removed at operation presented no evidence to suggest that the deposit of iron pigment is a frequent cause of hyperthyroidism

The case of a girl, aged $6\frac{1}{2}$ years, with two outstanding symptoms, an enlarged heart and hirsuties, is reported by I P Bronstein and J J Baratz 115 The diagnostic and therapeutic problems confronted in this case are discussed and the less common causes for cardiac enlargement in children are reviewed The heart decreased in size on the administration of desiccated thyroid and returned to the original enlargement when this medication was stopped With the resumption of the administration of thyroid, the heart returned to approximately normal measurements. The maximal change was over 19 inches (5 cm) in three months. These changes in the size of the heart are characteristic of myxedema heart and it is suggested that the name "accordion heart" be employed for the condition. The hirsuities was not affected by administration of thyroid

Parathyroid Gland

The relationship of parathyroid and kidney disease has aroused great interest among the investigators J D Barney and E R Mintz¹¹⁶ have discussed the relation of the parathyroid to urinary lithiasis. According to these authors hyperparathyroidism is responsible for between four and five per cent of all cases of urinary stone. The percentage of

stones in the presence of this disease may be almost 70 per cent. In about 38 per cent of cases of hyperparathyroidism the patients may show both bone and urinary tract pathology. The symptoms and signs of urinary lithiasis in parathyroid tumor do not differ from those due to other causes. In all cases of urinary lithiasis a careful study of the calcium and phosphorus content of the blood should be done.

In previous papers B Chown, M. Lee and J Teal¹¹⁷ have reported some of the lesions in the human kidney resulting from excessive calcium excretion It was suggested that the kidney lesions in some cases of renal rickets and chronic pyelonephritis are primarily the result of injury by calcium To examine the effects of mineral injury on the kidney, experimental studies on animals were undertaken In this series of experiments, certain lesions produced in the kidneys of rats after the injection of Collip's parathyroid extract are described Intratubular deposits, coarse, circumscribed, interstitial deposits, extrusion of calcium into the tubules with pus formation and fine diffuse interstitial deposits of calcium were found in the experimental animals

Effect of experimental reduction of kidney substance upon parathyroid glands and skeletal tissue has been studied by A M Pappenheimer 118. This experiment showed that reduction of renal tissue in young rats regularly leads to a marked increase in the volume of the parathyroid gland. If partially nephrectomized rats are maintained on a low calcium diet, growth is stunted and skeletal lesions are produced of far greater severity than can be ascribed to the dietary calcium deficiency alone. The picture closely resembles that found in cases of renal rickets in children.

T. G Drake, F Albright and B Castleman¹¹⁹ have produced hyperplasia in the parathyroid glands of rabbits by the parenteral administration of phosphate While the average weight of the inferior pair of parathyroid glands of 19 control rabbits was ½ grain (13 mg). the corresponding figure for 19 rabbits which had received injections of parenteral phosphate three times daily for one to 108 days was $\frac{5}{16}$ grain (20 mg) The parathyroid glands of the injected animals showed definite histological evidence of hyperplasia The findings support the hypothesis that phosphate retention is the cause of the parathyroid hyperplasia in cases of chronic renal insufficiency It will require further study to show whether the hyperphosphatemia causes the hyperplasia directly or indirectly by producing a hypercalcemia

In an attempt to determine whether the hyperplasia of the parathyroid gland noted in nephritic patients is accompanied by a hyperfunction of these glands, W J Highman, Ir, and B Hamilton¹²⁰ have examined the activity of the parathyroid glands by applying the method of Hamilton and Swartz Blood from each of 23 nephritic patients was injected into rabbits and the rise of the serum calcium of the rabbits was determined The blood of all but three of these 23 patients produced a rise of more than 03 mg of calcium per liter of rabbit serum which indicates that more than normal amounts of parathyroid hormones were present in the injected blood. It was found that there is no direct correlation between the degrees of hyperactivity of the parathyroid glands, as measured by this procedure, and the amount of elevation of the serum phosphorus, nor is there a direct relationship between the parathyroid activity and the blood urea nitrogen According to Pappenheimer and Willens it is probable that the cases with severe clinical nephritis have phosphate retention and since any increase in PO₄ ions will decrease the amount of calcium ions in the blood, this may incite the parathyroids to increased activity and overgrowth The findings of Hamilton and Highman seem to support this assumption

C E Snelling and A Brown¹²¹ have reported severe cases of tetany in the newborn The calcium level was found to be between 39 mg per 100 cc and 77 mg per 100 cc The symptoms common to these cases were twitching, spells of cyanosis and convulsions In no case was a crow observed or Trousseau's or Chvostek's signs Tetany is reported to be a common cause of cyanosis in the The treatment consisted of calcium gluconate injected intramuscularly, and calcium chloride and viosterol by mouth. Since tetany in the younger age group has been emphasized, the peak of the age incidence of tetany has changed from four to ten months to a much younger age

A case of hyperparathyroidism due to carcinoma of the parathyroid gland is described by A M Snell 122 The calcium was elevated to 149 mg per cent, the phosphorus was lowered to 26 mg per cent and the serum phosphatase showed an elevation to 24 Bodansky units per 100 cc The bones of the thorax showed marked osteoporosis with multiple spontaneous fractures of the ribs It is of interest to note that this condition was combined with a marked polyuna The average output of urine was about 100 ounces (three liters) a day The urine contained traces of albumin The renal function was greatly reduced The value of blood urea averaged 40 mg per cent The tumor was removed, on re-examination seven months after operation the patient showed a marked improvement

He had gained more than 40 pounds (182 kg) The serum calcium was 94 mg. per cent, serum phosphorus 3 mg per cent and the serum phosphatase value nine Bodansky units per 100 cc

A Rados and L. C Rosenberg¹²³ have discussed the relation between blue scleras and hyperparathyroidism In the usual cases of blue scleras associated with spontaneous fractures and hereditary deafness there are not sufficient variations in the values of calcium, phosphorus and phosphatase to warrant the supposition of involved endocrine disturbance In osteogenesis imperfecta there is evidence of decided hereditary transmission in contrast to hyperparathyroidism which shows no such influence Osteitis fibrosa cystica is based on hyperactivity of the parathyroid glands, the usual cause being tumor formation within the glands resulting in mobilization of the supply of calcium The spontaneous fractures occur in adult life and are accompanied by negative calcium balance, cyst formation and giant cell tumors of the bones The small minority of cases in which blue scleras are associated with true parathyroid disorder are rare exceptions, the pathologic features not constituting the usual picture The most plausible explanation lies in the possibility that the condition of hyperparathyroidism has been superimposed on a preexistent congenital anom-Similarly, spontaneous fractures are clinical features of the other form of generalized osseous disease, osteogenesis imperfecta associated with blue scleras and deafness. They occur in utero or in infancy or in childhood in contradistinction to the adult age incidence of hyperparathyroidism The roentgenographic picture of the osseous condition is that of osteoporosis There are absence of a negative calcium balance and lack of

increased phosphatase activity in osteogenesis imperfecta, the latter being a distinguishing feature of the parathyroid syndrome Furthermore, blue scleras are characterized by dominant hereditary transmission and are due to a congenital faulty differentiation or malformation of the mesenchyma

A rare and very interesting case report on hyperparathyroidism in siblings is made by L Goldman and F S Smyth 124 In both cases, the sister, 17 years old and the brother, 23 years old, generalized osteitis fibrosa cystica was found The clinical, metabolic, blood chemical and roentgenologic findings were those of the classic type of Recklinghausen's disease In both cases there was evidence of hypercalcemia Conversely, the phosphorus was lower than normal In the first case the phosphatase was definitely elevated, in the second it was not so obviously so and the authors were inclined to correlate this with the lessened involvement of bone, masmuch as the amount of phosphatase is an index of the activity of bony metabolism. One patient had renal calculi, the other did Both patients were successfully treated for hyperparathyroidism associated with generalized osteitis fibrosa cystica by the surgical removal of parathyroid adenomata After their removal, the clinical symptoms disappeared and the blood and metabolism became normal This case is of interest because hyperparathyroidism is usually not considered to be a familial disease

Suprarenals

An experimental study of the effect of diphtheria toxin upon vitamin C in adrenals of guinea pigs has been undertaken by C C Torrance 125 The adrenals of guinea pigs injected with a uniform lethal dose of diphtheria toxin were examined for their vitamin C content

The vitamin C content of the adrenals of the guinea pigs which had died from the effects of the diphtheria toxin was reduced to less than 15 per cent of that of the control animals. The animals that received only half the lethal dose showed much less change. The average amount of vitamin C in these animals was 85.8 per cent of that of the normal controls. Some animals which were sacrificed 48 hours after injection showed an increase in the vitamin C content of their adrenal glands.

The influence of sex hormone on vitamin C content of suprarenals and liver of guinea pigs has been studied by J Mosonyi ¹²⁶ It was found that the male as well as the female sex hormone reduces the vitamin C content of the examined organs of animals of the same sex at an average of 30 to 40 per cent. The male sex hormone was not effective on female animals while the follicular hormone had a definite effect on male animals.

H Bruch and D J McCune¹²⁷ have investigated the involution of the adrenal alands in newly boin infants Determinations of the sodium content and the specific gravity (protein content) of the plasma, the cell volume and nonprotem nitrogen content of the whole blood and the amount of total base in the plasma were made on seven samples of blood from the umbilical vein and in 106 specimens of venous blood obtained from 72 healthy infants within the first three weeks of life Despite the temporary increase which these infants exhibited with reference to the volume of erythrocytes and the level of plasma protein, the concentration of sodium and the total base in the plasma remained normal and constant during the period of study at levels identical with those found in healthy children and adults The concentration of nonprotein nitrogen was inconspicuously elevated during the first few days of life At no time was it high enough to suggest functional insufficiency of the adrenal cortex. In newly born infants during the period when rapid involutional changes are occurring in the cortex and the adrenal glands the authors have been unable to demonstrate biochemical changes of the sort found in human beings with Addison's disease or in animals deprived experimentally of the adrenal cortex.

An investigation of the pathologic alterations in the *lipoid content of the adrenals* in infancy and in childhood has been made by M. L. Menten and M. P. Smith ¹²⁸ Wide variations in the lipoid content of the cortex were observed in adrenals from 70 patients. The most marked depletion occurred in infections of long duration. Comparison of the vitamin C concentration of one adrenal with the histochemical lipoid content of the second adrenal in nine cases showed a corresponding reduction of the two substances.

W M Firor¹²⁹ has reported a case of *intestinal bleeding* which lasted for several months and finally ended in a fatal circulatory collapse with hyperpyrexia. The autopsy made clear the cause of these two final conditions. An infected cavity in the pancreas communicating with the pancreatic duct was found as the obvious source of the bleeding into the gastrointestinal tract and extensive hemorrhages destroying both adrenals explained the collapse and death of the patient. The author discusses the causes of adrenal hemorrhages in children

A report of two cases of fulninating septicemia associated with purpura and bilateral adrenal hemorrhage (Waterhouse-Friderichsen syndrome) with review of the literature has been made by M S Sacks ¹³⁰ The clinical picture of a rapidly fulninating septic course asso-

ciated with a marked purpura was considered of sufficient definiteness to warrant consideration of the syndrome as a clinical entity. The outstanding pathologic finding was bilateral adrenal hemorrhage, usually of a massive type. The review of the literature revealed a total of 64 cases, 70 per cent occurring in children below the age of two years, 21 case reports mentioned bacteriologic etiology. Of these, 60 per cent were of meningococcic origin, the remaining 40 per cent were due to streptococcus hemolyticus or the pneumococcus or were reported sterile after careful examination.

J. W Camerer¹³¹ has described a case of adrenal cortical insufficiency following scarlet fever The case of scarlet fever concerned was relatively mild without toxic symptoms and its course was without complications The first symptoms which were interpreted as adrenal cortical insufficiency appeared about two weeks after the onset of the disease These symptoms were adynamia, prostration and vomiting There was also a mild decrease of blood pressure There were several crises for the worse and the appearance of pigmentation patient finally died and an autopsy was performed Severe changes of the suprarenal glands were found Macroscopically, they showed an intensively yellow cortex Microscopical examination showed both suprarenal glands equally affected A fatty necrosis in all layers of the adrenal cortex was found some places there were also reparative processes with the formation of polynuclear giant cells around cholesterol crystals The capsule was found to be The picture was that of a cytotoxic contracted, suprarenal gland

A case of carcinoma of the adrenal cortex has been reported by A A Little¹³² in a child $7\frac{1}{2}$ years old The following symptom complex was found Virilism,

hirsutism, adiposity, precocious development, voice change, hypertension and hypertrophy of the clitoris and external genitals associated with hyperfunction of the adrenal gland It is of interest to note that the parents noticed that the child was rather large for her age as early as 31/2 years At the age of 41/2 years she began to appear heavy and large Hair could be seen on the body and face and the habitus became that of the male Pubic hair at this time was extensive and there was hypertrophy of the external genitals She was brought to the hospital in convulsions and finally died of pneumonia Autopsy revealed carcinoma of the cortex of the suprarenal gland Metastases were found throughout the lobes of both lungs and in the liver Only the left suprarenal gland was involved, the right suprarenal gland was small and atrophic The remaining glands of internal secretion were found to be normal

M A Goldzieher and S B Barishaw 133 have discussed a case of Addison's disease due to atrophy of the adrenal glands in which transplantation of adrenal tissue was attempted. The patient was kept alive by administration of salt and cortical extract for a period of over two years Interienin seemed to give the best relief Adrenal tissue obtained from a case of hypercortical syndrome was transplanted into the rectus muscle The patient survived for a period of nine months in comparatively good health After this period he was brought to the hospital in an almost moribund condition Autopsy revealed complete absence of the original cortical tissue but survival of the transplanted cortical tissue in a morphologically adequate state of pres-The technic and chances of ervation cortical tissue transplantation in Addison's disease were discussed by the authors The use of a donor of the same blood group and stimulation of the graft by injections of the pituitary corticotropic principles were suggested

The treatment of undescended testes with anterior pituitary-like substance is still interesting the clinicians W O Thompson, A D Bevan, N J Heckel. E. R McCarthy and P K Thompson¹³⁴ have observed the effects of treatment with anterior pituitary-like substance (from the urine of pregnant women) on 21 undescended testes in 18 boys from 11/2 to 17 years of age In eight instances the testes were intra-abdominal and in 13 inguinal The dose of A P L substance varied but was usually about 200 rat units three times a week for an average of five months The descent occurred in four patients or 19 per cent. In all four cases the testes were in the inguinal canal before treatment and in two could be pushed to the upper end of the scrotum Descent occurred within one month In one of these four cases the testis returned to the inguinal canal when treatment was stopped In seven other patients treated surgically after prolonged administration of A P L substance anatomical factors making descent difficult or impossible were present However, preoperative treatment with this material caused definite stimulation of genital growth and thus seemed to make surgi-Operative cal procedure less difficult procedures appear to be necessary in most cases of undescended testes, but in the present state of our knowledge should be preceded by from four to six months of treatment with A P L substance

A similar study has been undertaken by C van Gelderen ¹³⁵ Hormonal treatment with *pregnancy urine extract* was administered to 70 boys with undescended testes. The author thinks that cases in which the testes are not descended bilaterally are promising. Fivesixths of the cases responded to the treatment, one-half bilaterally and one-

third unilaterally Cases of unilateral nondescent are not very promising Onethird was cured

A J. Cramer, Jr., 136 has summarized the published case reports of hormonal therapy for undescended testes and has included 20 cases of his own, making a total of 81 cases in the literature. Analysis of the results shows that a complete descent of the testes was obtained in 71 6 and a partial result in 16, making a total of 87.6 per cent who were benefited by this method of therapy. The evidence is sufficient to consider hormone treatment a valuable method of therapy for undescended testes When surgical correction is indicated, the results may be enhanced by the use of hormone therapy as an adjunct

M A Limper and E E Hieronymus¹³⁷ have reported four cases of gonorrheal vaginitis treated with an ethylene glycol solution of amniotin. There were two permanent cures and two recurrences With oily solutions of amniotin or of progynon-B administered intramuscularly twice weekly conversion from the infantile to the adult type of vaginal mucosa was observed and cures were obtained in all except two cases. One patient treated with folliculin menformon daily for 60 days failed to respond to treatment. No harmful effect as a result of the injections was observed.

H Jacobziner and A Gorfinkel¹³⁸ have described three children with abnormal development of the genitalia. This report is of special interest because the three children were siblings, there were no other children in the family. The parents were normal in appearance and behavior. The family history was negative. The first child, a boy, was first seen at the age of 4¾ years. He was a tall child, and appeared entirely normal except for the development of the genitalia. The penis was very large, approximating

that of a normal adult, and the testes and prostate also were like those of a normal adult. There was a moderate growth of long pubic hair of male distribution. The growth of hair was first noticed by the parents at the age of 18 months. The second child, a girl, was seen at the age of three years when she already appeared like a girl of six years. She showed, otherwise, normal findings except for



 F_{1g} 2—M M, aged 41/2 years, with a penile-like clitoris which is the size and shape of a penis of a boy 5 years of age A moderate growth of pubic hair is shown There was a marked increase in height (Courtesy, Amer J Diseases of Children, August, 1936)

marked hypertrophy of the clitoris approximating in size the penis of a boy of her age. There was some hair of male distribution over the pubic region. This hair was already noticed at the age of 16 months. The hypertrophied clitoris, however, was seen at birth and for several days there was a question of sex. Both children were mentally rather dull. The third child was seen at the age of seven months. She looked well developed and

more alert mentally than the children previously described. The body build was normal in all proportions was a penis-like clitoris the size of a penis of a boy of the same age. The hypertrophy of the clitoris in this case was also noted at birth The author pointed out that this syndrome in many cases is dependent not upon the size of the gland nor on the presence of a tumor but on the character of the cells of the cortex It is a qualitative rather than a quantitative factor Unilateral adrenalectomy at puberty would seem to the author the procedure of choice in cases of this type in girls

Three cases of typical hypergentalism (macrogenitosomia) appearing in one family have been reported by H P Rush, J B Bilderback, D Slocum and A Rogers ¹³⁹ Male sex hormone was demonstrated in the urine of each of the three by use of the capon-comb test. Normally this is not found in boys under ten years of age. Prolan could not be demonstrated by the action of urine extract in immature female rats in any of the cases. No associated signs or symptoms

were present from which to suspect tumor or marked hypertrophy of the pineal, adrenal cortex, gonads, pituitary or thymus There were no signs or symptoms from which a cerebral lesion might be suspected. These cases seem to fall in the group called primary or congenital pubertas praecox. In addition to the three cases reported, the family history disclosed five other instances in four generations. The condition seems, therefore, to have been genetically determined. It is possible that what was inherited may have been an abnormal responsivity to gonadotropic hormones.

According to P Rosenblum, 140 puberty mastitis has definite characteristics It is always behind the nipple and occurs in girls between 8 and 12 years of age and in boys between 14 and 18 years. It is probably caused by some endocrine disfunction and local trauma may play a rôle. Pathologically, it is a pericanalicular and periacinous infiltration with connective tissue and lymphocytes together with epithelial hyperplasia. The condition is benign and disappears within a few months.

GENITOURINARY SYSTEM

By Waldo E Nelson, AB, MD

ENURESIS

Favorable experience with the use of sodium chloride (after the plan of Krasnogorski) in the treatment of nocturnal enuresis in children is reported by W Rosenson and R Liswood ¹⁴¹ The following is their plan for the daily régime with this treatment. The child is permitted a regular diet for breakfast and lunch. Fluids are permitted freely until noon, after that they are somewhat limited until 4 P M. At that time the last

drink of water or milk is offered until the following morning. Supper is at 5 30 P M and consists of food containing as little water as possible. Such i diet includes meat, fish, eggs, bread, butter, cheese and crackers. No vegetables, fruit or cereal are permitted. After the child is in bed for the night he is given a salty sandwich. Examples of the sandwiches prescribed are listed in Table 1. It believed that the salt is most effective when combined with fat or meat, when it

TABLE 1

| Sandwich Fillings | Quantities | Grams of Salt |
|---|--|--------------------|
| Bacon. Salt butter Salt | 6 strips 2 teaspoonfuls ½ teaspoonful | 0 5 to 1 2 |
| Boned herring Salt butter (Chopped hard-boiled egg) | 30 gm 2 teaspoonfuls | 5 0 5 to 1 |
| Ham . Swiss cheese Salt butter Salt | 45 to 50 gm 30 gm 2 teaspoonfuls 1/4 teaspoonful | 2 2 1 2 |
| Boneless salt codfish | 35 gm | 4 to 5 |
| (Raw scraped apple) Salt butter • | 2 teaspoonfuls | 0 5 to 1 |
| Smoked salmon Salt butter | 45 to 50 gm 2 teaspoonfuls | 4 to 5 0 5 to 1 |

(Courtesy, Journal of Pediatrics, December, 1936)

is absorbed gradually and the restraining influence on the discharge of urine is prolonged

Acute Hemorrhagic Nephritis

An ultimate mortality of 40 per cent for children who have had acute hemorrhagic nephritis is said by A W Snoke¹⁴² to be a conservative estimate This is based upon follow-up studies on 154 children who had this disease, and is in distinct contrast to the general belief that children who do not succumb during the acute stage of hemorrhagic nephritis recover completely According to Snoke it is the failure to recognize the existence of a latent stage following the acute attack of hemorrhagic nephritis which explains the fact that a good many instances of chronic nephritis that end fatally are not associated with acute hem-The latent stage is orrhagic nephritis usually not detectable by the ordinary urinalysis or by kidney function tests Snoke is of the opinion that the only method for demonstrating the existence of this latent stage is the quantitative examination of properly concentrated urine according to the method of Addis (see Table 2 for the calculated normal range of formed elements and protein per 12hour period) It is suggested that failure to employ this method often leads to such erroneous conclusions as: (1) That the patient does not have nephritis, (2) that he has completely recovered from an acute attack, (3) that small amounts of albumin, casts or red blood cells in the urine, when found, are without serious significance, (4) that patients who have had acute hemorrhagic nephritis usually recover completely without residual symptoms, and (5) that chronic "nephritis" terminating in uremia is unconnected with acute hemorrhagic nephritis contrast, Snoke believes that hemorrhagic nephritis, commonly if not invariably, enters a latent stage after the initial one It is pointed out that the evidence of Addis and Lyttle suggests that the initial stage in some instances may be so mild that it passes unnoticed However, it is believed that even subclinical acute hemorrhagic nephritis often passes through a latent stage and eventually terminates fatally Latent hemorrhagic nephritis may

| TABLE 2 | | | |
|-----------|-----|--------|-------|
| Excretion | Per | Twelve | Hours |

| | Average | Minimum | Maxımum | Suggested Upper Normal |
|--|------------------------------------|----------------------|--------------------------------------|--------------------------------------|
| Addis Casts Red blood cells White and epithelial cells Protein (albumin), mg | 1,040 65,750 322,500 30 | 0 0 32,400 | 4,270 425,000 1,835,000 | 5,000 500,000 1,000,000 30* |
| Lyttle Casts Red blood cells White and epithelial cells Protein (albumin), mg | 1,085 15,181 322,000 18 5 | 0 0 9,000 3 | 12,016 129,000 2,822,000 47 | 10,000 600,000 1,000,000 35 |

^{*} On the basis of larger experience this figure will probably be increased to ±60 mg (Courtesy, American Journal of Diseases of Children, March, 1937)

terminate in healing or may pass on to the degenerative stage or to the terminal stage and its duration is enormously variable. The later stages may not occur until some time in adult life.

The prognosis for the successive stages of glomerular nephritis - active, latent, degenerative and terminal-is progressively worse, the last named being uniformly fatal No prognostic significance could be attached to the age at the onset or at the time of the detection of nephritis It was found that hypertension and increased amounts of blood usea tended to parallel one another. In the initial stage there was no relation to prognosis, but when they appeared in the later stages they supplied the first indication that the patient was entering the terminal stage of renal insufficiency. The value for blood urea was not found to be abnormally high as a general rule until 50 per cent or more of the renal tissue failed to function In only two instances, both slightly doubtful, did any of the children in this series recover from a nephritis that lasted more than two years Snoke states emphatically that glomerular nephritis cannot be considered to be healed until repeated quantitative examinations of concentrated urine (Addis' method) over a period of at least one year have been normal

The observations and conclusions of H H Boyle, C A Aldrich, A Frank and S Borowsky143 are in distinct contrast to those of Snoke Quantitative determinations by the Addis method were made on 25 children who had clinically recovered from acute postinfectious, hemorrhagic nephritis for periods of from one-half to eight years With the exception of the determination on one girl who was found to have a hydronephrosis, the figures obtained corresponded very closely to those obtained from normal children Pathologic sediments were not found when determinations by the ordinary clinical and laboratory procedures were within normal limits The authors conclude that their results are further evidence in favor of the view that children who have clinically recovered from acute postinfectious, hemorrhagic nephritis do not have subacute or latent nephritis. They interpret clinical recovery as indicated by the absence of all known symptoms and signs of nephritis, as well as by completely negative urinalyses

Nephrosis

Because of the frequency of pneumococcic peritonitis as a terminal infection in nephrosis and the contention of Blackman and others that nephrosis is a result of pneumococcic infection, S C Peacock and M Werner¹⁴⁴ have studied a group of children with nephrosis from the standpoint of their humoral immunity against the pneumococcus An investigation into the value of systemic and local immunization in the prevention of terminal pneumococcic peritonitis was also carried out No noteworthy differences were found between the humoral antibodies against Types I and II pneumococci in the blood of nephrotic children and the humoral antibodies against Types I and II of pneumococci in the blood of normal chil-Strains of pneumococci isolated from the peritoneal fluid or material from the throats of children with nephrosis were of Group IV with the exception of one strain, Type II In individual cases the strain from the throat always differed from the strain in the peritoneal fluid of the same patient Pneumococci were not isolated from any of eight vaginal cultures from four nephrotic and four nor-No correlation could be mal children determined between the agglutination titers of the serum of immunized animals and the resistance of the animals to intraperitoneal injection

Renal Rickets

In a discussion of the etiologic factors of renal rickets, B Chown and M Lee¹⁴⁷ state that there are three probable causes (1) Chronic nephritis, or malformation of the urinary tract, with renal failure and consequent simple rickets due to chemical imbalance, (2) primary or secondary hyperparathyroidism, and (3) primary diencephalopituitary lesion. The authors believe the latter to be the common cause and suggest that the parathy-

roid enlargement in some instances is due to a primary pituitary lesion They point out the necessity of finding a factor which will satisfactorily explain (1) Polyuria, (2) dwarfing; (3) infantilism, (4) lability of the blood calcium and phosphorus levels; (5) destruction of the kidneys, and (6) faulty growth of the bone It has been definitely shown that disease of the pituitary diencephalon will account for the polyuria, dwarfing and infantilism There is also experimental evidence suggesting that disturbances of the diencephalum may account for abnormal calcium and phosphorus metabolism B Chown has shown elsewhere 146 that hypercalcemia may account for kidney destruction

Kidney Function Test

A comparison of the xylose tolerance test with blood urea retention in nephritic rats has been made by H W Larson 147 This work is of interest particularly as it relates to that of Fishberg and Friedfeld, who have advocated the use of the xylose test as a delicate index of damaged renal function Larson induced nephritis in rats by feeding a diet containing 43 per cent dried liver results were consistent with the view that kidney function must be seriously disturbed before there is retention of urea The degree of nephritis produced was not sufficient to cause marked histo-The values for blood logic changes xylose indicated that the use of this sugar as a delicate index of renal function was open to serious question Furthermore, the author was unable to obtain consistent xylose values in a group of nonnephritic rats. In many instances the results obtained with xylose would indicate that one month some of the normal rats were definitely nephritic and the next month normal, and so forth, since the xylose values were high at times and

at other times were at the fasting level On the basis of this work, Larson believes that the excretion of albumin and the presence of casts in the urine are the earliest indicators of renal disturbance

Lower Urinary Tract Infection

Treatment—As pointed out by H F. Helmholz, 148 two drugs, mandelic acid and sulfanilamide, which are extremely valuable in the treatment of urinary infections, have been introduced within the past two years. Mandelic acid is an adequate substitute for the ketogenic diet. However, they can be used only in the subacute and chronic stages of pyelitis, whereas sulfanilamide can be administered in the acute febrile stage.

Mandelic acid acts bactericidally in about the same concentration and in the same range of pH as beta-oxybutyric acid Each requires organic acid concentrations of from 05 to 10 and a pH of the urine between 50 and 55 Anything that prevents the achievement of these treatment conditions invalidates the Thus mandelic acid is not effective unless the function of the kidney is normal or nearly so In infections with urea-splitting organisms, such as those of the proteus group, the alkalimity of the urine is usually such that, in spite of the use of acid salts, the urinary pH rarely approaches 55 It has been shown that mandelic acid acts bactericidally on all the common gram-negative bacilli found in urinary infection as well as on staphylococcus aureus and streptococcus fe-Mandelic acid was administered originally as the sodium salt together with ammonium nitrate or ammonium chloride to acidify the urine, but is now generally given in the form of the ammonium salt If the urine does not reach the necessary pH of 55, ammonium nitrate may be given in addition. The mandelate is almost quantitatively excreted in

the urine, so that by knowing the amount given in 24 hours and the total daily output of urine, the concentration of mandelic acid in the urine can be kept at approximately one per cent The usual adult dosage is 3111 (12 grams) a day, that is, 45 grains (3 grams) four times a day, taken after each meal and at bed-The 24-hour quantity of urine should be kept at about 1 quart (1000 For children, the dosage is proportionately smaller Fifteen grains (1 gram) of ammonium mandelate is prescribed for each 100 cc of urine in the daily output Accordingly, for an output of 1 pint (500 cc), 75 grains (5 grams) of the drug should be given In addition to the proper urinary concentration of mandelic acid, it is necessary to have the proper acidity, and this should be determined daily If the necessary acidity is not reached by means of the administration of ammonium mandelate alone, ammonium chloride or ammonium nitrate in doses of from 71/2 to 30 grains (0.5 to 2.0 Gm) four times a day should be administered

Helmholz has been able to show that a sufficient concentration of sulfanilamide in the urine may be obtained by oral administration to make the urine bactericidal for staphylococcus aureus, escherichia coli, aerobacter aerogenes and organisms of the proteus and pseudomonas groups This drug, however, has no bactericidal effect on streptococcus fecalis In contrast to mandelic acid, sulfanilanude is more effective in alkaline than in acid urine After the administration of sulfanilamide, the urine is usually alkaline, but it is important to determine that such is actually the case Sulfanilamide may be given together with sodium bicarbonate and sodium citrate The dosage of sulfanilamide in infancy is from 5 to 10 grains (03 to 065 Gm) a day, for children from two to four years of age, 10 to 15 grains (0.65 to 1 Gm.); for children from four to eight years, 15 to 25 grains (1 to 16 Gm), for children from 8 to 12 years, 20 to 30 grains (13 to 2 Gm) a day. Helmholz states that sulfanilamide, because of its ease of administration and tolerance by the stomach is the drug of choice. It also has the added advantage that it can be used during the acute stage of the disease. Thus these two drugs, mandelic acid acting only in an acid medium and sulfanılamıde in an alkalıne medium, supplement each other, and they should be used in the treatment of urinary infections according to the type or types of invading organisms

Good results with the use of *prontosil* in the treatment of pyelitis in children is also reported by W Pernice 149 The dose employed for infants was 1½ grains (0.1 Gm.) three times a day by mouth, for small children, 2½ grains (0.15 Gm.) three times daily, and for older children, 5 grains (0.3 Gm.) twice daily. Normal urinary findings disappeared within 4 to 11 hours. However, the author recommends that treatment with prontosil be used for eight days after the disappearance of the abnormal symptoms.

Obstruction of Lower Urinary Tract

Increasing evidence of the frequency of obstructive lesions of the lower urmary tract in children has demonstrated the importance of early corrective procedures. One of the causes of obstruction of the ureter may be reduplicated or aberrant blood vessels of the kidney. This subject has been discussed by M. F. Campbell 150. Two explanations have been advanced for ureteral obstruction by aberrant vessels. The opinion of the minority is based on the assumption that the vessel primarily compresses the ureter. The majority maintain that the

obstruction follows an initial renal ptosis which causes the ureter to sag over the vessel or occasionally over a periureteral fibrous band. Thus it is stated that in a large proportion of instances, peripheral ureteral obstruction, notably at the ureterovesical junction is demonstrable The resulting hydronephrosis initiates the renal ptosis and the ureter, dilated as a result of an obstruction in its distal segment, compresses itself against the anomalous vessel and dilatation above this point is increased The most common manifestations are pain in the renal region, pyuria, hematuria, a mass in the loin and with the advent of infection, fever. In the absence of infection, the renal changes as interpreted by urinalysis usually result in a diagnosis of chronic interstitial ne-The correct diagnosis should usually be made preoperatively by a complete urologic examination, particularly the excretory urographic findings The treatment is surgical Conservative surgical treatment may be expected to save a number of kidneys However, delay in diagnosis usually necessitates a nephrectomy

Lithiasis

H L Kretschmer¹⁵¹ has summarized his clinical experience with stones in the urinary tract of children. In his series of 21 children the age incidence was from 1 to 12 years inclusive. Fifteen of the children were boys and six were girls. The locations of the stones is shown in the following table.

| | No of P | atients |
|--------------|----------------------------|---------|
| Stone in the | kidnev | 6 |
| Stone in the | | 3 |
| Stone in the | bladder | 7 |
| | kidney and the ureter | 2 |
| | kidney and the bladder | 2 |
| | kidney, the ureter and the | e |
| bladder | • / | 1 |
| | | _ |
| Total | | 21 |
| 2 | | - |

(Courtesy, American Journal of Diseases of Children September, 1936)

Twelve of the children had but one stone, while nine had multiple stones. In one instance, the retrograde movement of a stone was noted. (The author emphasizes the fact that all cases to be operated on for stones in the ureter should have a roentgenogram made just before operation, as the stones sometimes migrate up the ureter and even into the kidney pelvis.) The *symptoms* in this series of cases are shown in the following table.

| able | No of Cases |
|-------------------------|-------------|
| Pam | 19 |
| Frequency of urmation | 13 |
| Hematuria | 10 |
| Fever | 9 |
| Pain on urination | 9 |
| Difficulty of urination | 9 |
| Vomiting | 7 |
| Incontinence | 6 |
| Headaches | 6 |
| Cloudy urine | 5 |
| Burning on urination | 4 |
| _ | |

(Courtesy, American Journal of Diseases of Children, September, 1936)

An analysis of the urine of the 21 children in this series showed the presence at some time of one or more pathologic elements, such as red blood cells, pus cells, albumin, bacteria and crystals. In one instance the finding of crystals in the urine not only prevented an emergency appendectomy, but the type of stone was diagnosed by the type of crystals (cystine). Positive evidence of stones was obtained in all but one instance (stone in a diverticulum) by roentgenographic examination.

Three of the children passed the stones spontaneously In five instances stones were removed from the kidney by pyelolithotomy and in one by nephrolithotomy, in two instances resection of the kidney was also performed. Stones from the ureter were removed by ureterotomy. Five of the children with stones in the bladder were treated by suprapubic lithotomy, and five by lithola-

paxy If the stones are small enough to pass, if they produce only slight evidence of obstruction or none at all and if infection is mild or absent, medicinal management is justifiable. This consists in the administration alternately of urinary antiseptic and alkaline diuretics. The child should be encouraged to drink large quantities of water, milk, lemonade and other liquids

Actinomycosis of the Kidney

Actinomycosis of the kidney occurring in a girl ten years of age is reported by H L Kretschmer and W G Hibbs 152 The preoperative diagnosis was a tumor of the kidney, probably malignant There was a history of abdominal pain, lassitude and marked loss of weight Physical findings included a mass in the left upper quadrant of the abdomen, roentgenographic evidence of an enlarged kidney outline on the left side, urographic defects of the left kidney pelvis as revealed by pyelograms and sterile urine from the left ureter Left nephrectomy was performed and the immediate postoperative course was uneventful However, some five or six months later an abscess developed and ruptured at the site of the operative scar Actinomycoses were found in the smears from the draining sinus which persisted for 14 months. The child was given potassium iodide, from 75 to 100 grains (5 to 7 Gm) three times a day, and the fistulous tract was irrigated with a two per cent solution of copper sulfate In addition to these measures, five roentgen-ray treatments were given

The preoperative diagnosis of actinomycosis of the kidney is difficult and is most frequently confused with tuberculosis or tumor of the kidney. The preoperative diagnosis depends upon the demonstration of the fungus in the urine. It must be borne in mind, however, that

TABLE 3

Cases of Gonococcal Vaginitis Successfully Treated With Amniotin

| Cas e | Age— Years | Smear for Gonococci Before Treatment | pH Before Treatment | Duration of Treatment Days | pH After and During Treatment | Smear for Gonococci During and After Treatment | % Doederlein Organisms After Treatment |
|--------------|---------------|---|------------------------|-------------------------------------|--|---|---|
| 1 | 9 | + | 7 2 | 54 | 5 4 | negative | 0 |
| 2 | 3 | + | | 12 54 | 6 2 4 8 | still persists negative | |
| 3 | 3 | + | | 27 | 5 8 | negative | 0 |
| 4 | 4 | + | 8 0 | 13 | 5 6 | _ | |
| 5 | 7 | + | 8 0 | 13 25 | 6 0 5 2 | + negative | |
| 6 | 2½ | + | | 13 18 25 | 7 2 6 4 4 8 | + + - | |
| 7 | 2 | + | | 14 | 4 8 | _ | |
| 8 | 8 | + | 7 2 | 5 25 42 | 6 6 5 8 4 6 | + | |
| 9 | 2 | + | | 26 31 38 | 7 0 6 2 4 8 | + | |
| 10 | 5 | + | 7 8 | 13 20 | 7 0 4 0 | negative negative | |
| 11 | 3 | + | 7 6 | 13 19 | 7 0 6 2 | negative negative | |
| 12 | 5 | + | 7 2 | 12 | 4 8 | negative | |
| 13 | 2 | + | 7 8 | 14 | 5 2 | negative | |
| 14 | 5 | + | 8 0 | 25 | 7 2 | negative | 0 |
| 15 | 3 | + | | 28 | 5 4 | negative | 0 |
| 16 | 4 | + | | 24 | 5 2 | negative | 0 |
| 17 | 2 | + | | 14 | 5 8 | negative | 0 |
| 18 | 3 | + | | 34 | 4 8 | negative | 0 |
| 19 | 5 | + | | 48 | 5 4 | negative | 0 |
| 20 | 2 | + | | 16 | 5 0 | negative 7 | |
| 21 | 3 | + | | 17 | 5 0 | negative 8 | |
| 22 | 5 | + | | 33 | 5 4 | negative 7 | |
| 23 | 4 | + | | 36 | 6 0 | negative | 5 |
| 24 | 2 | + | | 29 | 4 8 | negative | 0 |

(Courtesy Surgery, Gunecology and Obstetrics, November, 1936)

actinomycotic abscesses may rupture into the urinary tract below the kidney. The persistence of a sinus after a nephrectomy for a chronic, suppurating process in the kidney in which tuberculosis of the kidney has been ruled out is an indication that the condition may be due to actinomycosis. Likewise the presence of a persistent discharging sinus in other parts of the body should lead one to suspect that the renal lesion may be due to actinomycosis.

Vaginitis

R M Lewis and L Weinstein 153 believe that the production of vaginal acidity is the important factor in the successful treatment of gonorrheal vaginitis with estrin Other explanations which have been offered as the factors responsible for the benefit from treatment with estrin (1) The exfoliation of the epithelium, supposedly aiding in throwing off the organisms and (2) the formation of a zone of cornification in the functional layer of the mucosa, thereby preventing penetration by the gonococci It has long been recognized that the natural acidity of the adult vagina tends to inhibit gonococcal infection When estrin is present, that is, at birth and very shortly thereafter, as well as from puberty to the menopause, the action of the secretions is typically acid, and the bacterial flora is predominantly of the bacillary type In the absence of estrin in childhood and after the menopause, there is a thin vaginal mucosa with a few layers of cells, an alkaline and nearly neutral reaction of the vaginal secretions and a mixed flora consisting essentially of cocci. The authors have determined the hydrogen ion concentration of the secretions of a number of normal children as well as of a series of children with gonococcal infections, before, during and after treatment In a series of 17 normal with estrin

children, the youngest of whom was four months of age and the oldest ten years, the vaginal secretions had an average hydrogen ion concentration of 72 The lowest value was 70 and the highest 74 The hydrogen ion concentration of the vaginal secretion of children with gonorrheal vaginitis before, during and after treatment with amniotin (75 r u gelatin capsules inserted in the vagina each night) are shown in Table 3 It will be noted that, in this series of cases, all of the hydrogen ion determinations made before treatment was begun were alka-In no case in which the vaginal secretions were found to have a hydrogen 10n concentration of 60 or below for any length of time could the gonococci be found in the smear after treatment

The authors describe their method for the determination of the hydrogen ion concentration of the vaginal secretions as follows Sterile physiologic salt solution is adjusted to a hydrogen ion concentration of 70, and 1 or 2 cc are expelled from a sterile pipette into the vagina and withdrawn several times to get a fair sample of vaginal washings The hydrogen ion concentrations of these washings are determined by the following indicators Brom-thymol-blue (pH 60 to 76), brom-cresol-purple (pH 52 to 66), and brom-cresol-green (pH 40 to 56) A drop of brom-thymol-blue is added to a drop of the vaginal washing An immediate change to a deep yellow indicates that the fluid has an acidity very near or greater than a hydrogen ion concentration of 60 If the resulting color is a very light green or shades into a heavy green or light blue, the reaction is more alkaline than the hydrogen ion concentration of 60

K J Karnaky¹⁵⁴ has had as satisfactory results with the use of acidulated sugar tablets in the treatment of vulvo-

vaginitis in children as he has had with ovarian hormone Sugar tablets with a pH of 30 to 33 were employed One sugar tablet is inserted in the vagina. two or three times a day, and no douches are given unless absolutely necessary If a douche is given, it is followed by insertion of two or three tablets. At the beginning of treatment the vaginal introitus is gently dilated, if small, with a well lubricated gloved little finger, or the hymen is incised If there is any difficulty in inserting the tablets, a small drop of lubricant, or contraceptive jelly may be used on the tablets to facilitate insertion After 30 days of treatment, the mother is instructed to irrigate the child's vagina three times a day with a solution made by adding three tablespoons of five per cent acetic acid to two quarts of warm tap water Irrigation is performed with an ear syringe

A preliminary report on the treatment of gonorrheal vulvovaginitis with a special hydrolyzed glucose tablet has been made by A A Little, Ir.155 The author's hypothesis for this plan of therapy was based on the assumption that the vaginal bacteria would increase the vaginal acidity by converting the glucose into lactic acid and thus inhibit the growth of the gonococcus The plan of treatment consisted in placing a tablet as far as possible into the vaginal vault morning and night No other treatment, except cleansing, saline douches when the discharge was profuse, was employed The author has treated 39 patients by this method and reports 19 as cured The remainder are still under treatment The suggestion is made that the combination of estrogenic substances with the glucose tablets might produce still better results

HEART DISEASE

By ROBERT A LYON, AB. AM, MD

Further attempts by Kaiser to evaluate the benefit of tonsillectomy seemed to show that the operation has no beneficial action in reducing the number of recurrences of rheumatic attacks, but the carditis in such children was apparently less severe and the mortality due to rheumatic fever was reduced to half of that of a control, untreated group

Treatment of chorea with artificial fever therapy has given better results with daily treatments than with treatments at intervals of longer duration

The sedimentation rate is believed to be of special value in the detection of subacute rheumatism and in determining the prognosis of the disease and of such related manifestations as subcutaneous nodules A comparison of various laboratory tests of the activity of a rheumatic infection showed that after the temperature and pulse rate returned to normal, the immature polymorphonuclear leukocytes disappeared slowly from the blood, and last of all the sedimentation rate returned to normal. From this it is argued that the sedimentation rate is the most accurate test of minimal activity of the infection and should be used to determine the length of time a rheumatic patient should remain in bed

Heart Disease in Children

Congenital Lesions—Congenital aortic atresia was reported in an infant who lived 20 hours, by J T Roberts 156 The patient had no symptoms at birth

but developed a cyanosis which gradually became deeper and was accompanied by dyspnea At autopsy the aortic atresia was found to be accompanied by initral stenosis, stenosis of the ascending aorta and arch, a patent foramen ovale, and enlarged ductus arteriosus The right ventricle was large and there was a dilatation of the pulmonary artery. Fifteen cases of a similar type have been reported previously in the literature with variations in the type of congenital abnormalities which accompanied the atresia of In the author's patient the the aorta aerated blood, which was small in amount, apparently passed from the left to the right auricle and was distributed in small amounts through the systemic circulation by way of the ductus arteriosus, which also supplied the coronary vessels for a short period of time The duration of life in such patients seems to be dependent upon the size of the opening of the foramen ovale The cause of the atresia has been attributed to inflammatory conditions in some of the previous reports but in the patient observed by the authors no evidence of inflammation could be found

Atresia of Tricuspid Valve—Among the other types of congenital atresia is atresia of the tricuspid valve which has been observed recently by J Brown 157 The child was cyanotic at birth and lived until the age of eight months when he died of bronchopneu-Associated with the atresia of the tricuspid orifice were defects in the septa between the auricles and between the ventricles The right auricle and the left ventricle were very large while the right ventricle was, of course, very atrophic These findings were demonstrated on the x-ray plates and together with the electrocardiographic changes showing left axis deviation helped to differentiate this condition from pulmonary

stenosis, which is the most common of the congenital lesions causing cyanosis at birth

Atresia of Pulmonary Orifice—An instance of atresia of the pulmonary orifice with an intact interventricular septum has been described by M M Steiner. Such a condition is incompatible with life and this infant was born dead. There was an atresia of the pulmonary orifice, a patency of the foramen ovale and the ductus arteriosus, but the ventricular septum was intact. Other congenital lesions in this infant were hydronephrosis and the absence of the external auditory canals and auricles of the ear.

Dextrocardia—Dextrocardia is a relatively rare condition and occurs from a variety of causes A summary of the subject has been presented by H A Reisman¹⁵⁹ with a review of eight patients presenting some of the different types The true congenital forms represent a transposition of the heart so that it appears in roentgenograms as a mirror image of the normal condition The liver, stomach, spleen and other viscera are often transposed also and the patient is usually free from symptoms The cardiac position can be diagnosed by physical examination, ioentgenograms and by electrocardiographic tracings which show a mirror image inversion in Lead I Some patients may have the heart transposed without the other viscera being involved, others may have congenital heart defects associated with the dextrocardia which give symptoms of circulatory disturbance Occasionally the heart is displaced towards the right side because of congenital defects of the diaphragm or lungs Finally, the heart may assume such a position because of acquired lesions, such as empyema or chronic pulmonary infections

Complete Extrusion of Heart-An unusual cardiac condition consisting of a complete extrusion of the heart from the thorax, with a developmental abnormality of the sternum, has been reported by C. E Kellet 160 The pericardium of the parietal fold and the ductus arteriosus were absent, and there was an incomplete development of the septa between the auricles and between the ventricles This patient lived only a few hours There are some 16 such cases reported in the literature and the duration of life is not more than 36 hours as an average Little effect or benefit is gained by trying to reduce the heart within the thoracic cavity because of the impairment of circulation which usually results Electrocardiograms made from this patient showed scarcely any deflection of the waves at all but nonpolarizable electrodes applied to the heart itself resulted in unusual types of electrocardiographic tracings The tracings were difficult to interpret but resembled in many respects those taken from experimental animals under The application of similar conditions cold to the surface of the right or left ventricle produced considerable changes in the waves of the electrocardiogram but the significance of the tracings was yet to be determined

Congenital Heart Disease — Congenital heart disease in more than one member of a family has been recorded, but more rare is the occurrence of an identical lesion in two sisters such as has been observed by D B Snelling ¹⁶¹ Both patients had evidence of a patent ductus arteriosus but the condition had not restricted their activity and both had had major operations without any cardiac disturbance during the process Important factors of care seemed to be the maintenance of good nutrition and health to avoid as far as possible the develop-

ment of subacute bacterial endocarditis or tuberculosis.

Rheumatic Heart Disease

Incidence - The incidence of heart disease in Philadelphia school children has been found to be 105 per cent. The survey was made by J. M. Cahan¹⁶² in one of the districts of a higher economic level in that city and included 33,293 children, of which number 157 were colored School physicians selected from the group 863 patients who had some abnormality of the heart From the re-examinations and the histories obtained from this group, cardiac lesions were demonstrated in 350 and definite organic heart disease in 191 The distribution of the cardiac lesions and their relative age incidence is shown in the accompanying tables

In the schools, careful efforts have been made to grade various types of activity from the highly vigorous competitive sports to the program of no exercise during a half day's school attendance Many difficulties confront the physician in grading the cardiac patient's functional capacity but constant observation and the co-operative efforts of the medical profession, the school officials and the family were considered to be highly essential in guiding the cardiac patient through his school years

A comparative study of the incidence of rheumatic heart disease among American Indian children was undertaken by J R Paul and G L Dixon ¹⁶³ Three groups of school children in the northern and southern parts of certain western states were selected because of similarities of race, customs, habits of living and the fact they were closely limited to reservation areas, rarely leaving their homes and not often visited by persons from the outside. The presence of apical or midcardiac murmurs together with

TABLE 1
HEART CONDITIONS IN SCHOOL CHILDREN SURVEYED

Total number of pupils' medical records reviewed

33,293

| Pupils with suspected cardiac abnormality nominated by school physicians for study Pupils for whom medical histories were obtained Abnormal symptoms or signs relative to the heart were found in Organic heart disease Congenital heart disease (including two having also acquired lesions) Acquired heart disease Class E Class F No heart abnormality 863 2 6 391 114 350 1 05 105 0 09 161 0 5 113 0 33 0 33 0 009 | | Number of Children | Per Cent |
|--|---|---|--|
| | for study Pupils for whom medical histories were obtained Abnormal symptoms or signs relative to the heart were found in Organic heart disease Congenital heart disease (including two having also acquired lesions) Acquired heart disease Class E Class F | 391 350 191 30 161 113 46 | 1 14 1 05 0 6 0 09 0 5 0 33 |

(Courtesy, Annals of Internal Medicine, June, 1937)

certain other factors of nutrition and general health was taken as a criterion of rheumatic infection. Rheumatic carditis was found to be about ten times more frequent among Indian children living in cold and relatively dry climates of Wyoming and Montana (4.5 per cent), as among those inhabiting the dry but warmer climates of Arizona (0.5 per cent). The possibility that the rheumatic infections of a mild character occurred more frequently in the south than shown by the presence of rheumatic carditis could not be substantiated by any evidence available to the authors.

Etiology—From an investigation of the relationship of the utilization of ceritamic acid to rheumatic fever, I Sendrov, Ir, and M P Schultz164 were unable to believe that deficiencies in vitamin C were the cause of rheumatic infections By use of the excretion tests for cevitamic acid, they observed a slight deficiency of that substance in eight of a group of 13 rheumatic patients which was very much like the results obtained in a control group They attributed the vitamin deficiency to factors of diet, vomiting, impaired absorption or possibly other nutritional or digestive disturbances. In some patients it may have been partly due to infection which may have depleted the stores of vitamins of all types. The clinical test of administration of cevitamic acid to rheumatic patients has not resulted in any appreciable improvement of the disease. M. P. Schultz¹⁶⁵ supplied cevitamic acid to one group of rheumatic children throughout a winter and spring season and observed that subclinical scurvy was prevented but no changes occurred in the incidence or the clinical course of rheumatic fever among that group as compared with an untreated control series.

The production of subcutaneous nodules similar in pathologic structure to those occurring spontaneously in patients with rheumatic fever has been accomplished by B F Massell, J R Mote and T D Jones 166 Two or 3 cc of blood were taken from 82 rheumatic patients and injected immediately into their subcutaneous tissue After about ten days of frictional pressure at the site of injection, 45 per cent of the group developed nodules which resembled true rheumatic nodules in their microscopic appearance The nodules occurred more frequently and were of larger size in patients with active rheumatic processes

| | Elementary School (ages 6 to 14 years) | | High School (ages 15 to 18 years) | | Total | |
|---|--|-----------------------|--------------------------------------|-------------------------------|------------------------|---------------------------------|
| Number of pupils on roll | 2 | 4,193 | 9,154 | | 33,293 | |
| Organic heart disease Class E Class F | No 111 74 30 | Per Cent 0 5 0 3 0 12 | No 80 39 16 | Per Cent 0 9 0 4 0 2 | No 191 113 46 | Per Cent 0 6 0 33 0 13 |
| Total abnormal hearts | 215 | 0 9 | 135 | 1 5 | 350 | 1 1 |

TABLE 2
HEART ABNORMALITIES IN YOUNGER AND OLDER CHILDREN

(Courtesy, Annals of Internal Medicine, June, 1937)

than in those with mactive lesions. In only one instance could such nodules be produced in a group of 34 non-rheumatic patients. The occurrence of nodules in a few rheumatic patients following the injection of saline was thought to be due to trauma and bleeding induced by the procedure.

Diagnosis - The differentiation of organic heart disease from functional disturbances by means of murmurs alone, has presented many difficulties A test devised by M M Maliner and I Okin¹⁶⁷ which seems to be of some assistance in making the diagnosis is the injection of six to eight minims of a 1 to 1000 solution of adrenalin which tends to accentuate the organic murmurs and to cause functional murmurs to disappear. In applying this test to a group of 32 children, the authors found that it was of considerable significance in all age groups but was most accurate in children over ten years of age The importance of such a test is indicated by a follow-up study of a series of children in which 62 per cent of the group were found to have developed organic heart disease after an original diagnosis of a functional heart murmur had been made The adrenalin test was compared in a group of 37 children with the results obtained with amyl nitrite inhalations and the authors concluded that adrenalin was the preferable drug for producing murmurs in cases of organic heart disease or of accentuating valvular murmurs which were present in mild degree only. The test, however, was considered to be only an adjunct to the other methods of diagnosis and such important measures as the continued observation of the patient and the various tests of the functional capacity of his heart and circulatory apparatus must be relied upon for the final diagnosis

A comparison of the value of Schilling counts and sedimentation rates as an index of the activity of rheumatic infections in children has been made by R R Struthers, H L Bacal, J Schacher and M Flander 168 Simultaneous tests in 100 children indicated that both tests varied from normal in patients with acute rheumatic infection chorea patients, however, neither was there a shift to the left in the Schilling hemogram nor an increase in the sedimentation rate of the red corpuscles It was in various stages of rheumatic carditis that the Schilling index was frequently normal when the sedimentation rate indicated a continuation of a pathological process Likewise, during and following tonsillectomy of rheumatic patients, the sedimentation rate showed considerable exacerbation of the rheumatic disease, while the Schilling

count was normal The Schilling index was found to be influenced more acutely by minor infections such as boils and sinusitis than was the sedimentation test.

Following the observation of the sedimentation rates of the erythrocytes of 140 children during various stages of activity of rheumatic infection, W M. Clifton 169 concluded that this test was an accurate measure of the status of that infection. The rate of sedimentation was increased in patients with active involvement of the joints or heart, including pericarditis with venous congestion, but the rate was often normal in patients with acute congestive heart failure Annular erythema and rheumatic nodules often associated with acute attacks of the illness were always accompanied by high sedimentation rates Chorea alone did The authors found not affect the test that a Schilling differential count also gave an indication of the presence of the rheumatic infection but was not as delicate a test as the sedimentation rate tor the determination of minute degrees of involvement and final disappearance of the infectious process. A typical attack of rheumatic fever as judged by the sedimentation test seemed to last about two months, which was at least two weeks longer than clinical evidence of the disease indicated

The value of sedimentation rate as an indication of the activity of a rheumatic infection has been confirmed by A F Coburn and E M Kapp ¹⁷⁰ It is the author's theory that a rheumatic attack begins with a preliminary streptococcic infection, is followed by a short asymptomatic period, and then flares up with an attack or exacerbation of rheumatic symptoms. In keeping with this idea, the sedimentation rate followed a similar course. An initial increase in the rate of sedimentation accompanied

the streptococcic infection of the nose and throat When no subsequent rheumatic attack occurred, the sedimentation rate subsided and remained normal When attacks of rheumatic fever developed, the sedimentation rates showed secondary rises just before or at the time of the rheumatic attack. The factors influencing the increase in rate of sedimentation of the erythrocytes seemed to be larger amounts of fibrinogen and globulin in the blood plasma Qualitative differences in respect to specific precipitins in these substances seemed to have no effect on sedimentation rates The author suggested that the large amounts of fibrinogen and globulin in the blood of rheumatic patients could be attributed to repeated stimulation of the reticulo-endothelial system by the foreign protein released into the patients' bodies by the rheumatic infection

An evaluation of the erythrocyte count and sedimentation rates in rheumatic fever has also been reported by F Massell and T D Jones 171 Their group was composed of 178 rheumatic patients varying in age from 3 to 27 years and in various stages of activity of their infection Leucocyte counts were considered to be inaccurate in many instances because of normal variations throughout the course of a Sedimentation rates were perdav formed by the Rourke and Ernstene method with corrections for cell volume Both tests usually indicated the presence of activity of the rheumatic process for several weeks after clinical evidence of the disease had subsided. In some patients one test was positive and the other normal and occasionally both were normal during acute rheumatic activity Other illnesses, such as respiratory disease or tonsillectomy, affected the tests for several weeks and such intercurrent infections had to be considered when abnormal readings were obtained. The authors concluded that the presence of persistent elevations of the leukocyte counts or of the sedimentation rates indicated an active infection, which, in rheumatic patients with no other sign of disease, were the result of the rheumatic infection itself.

Difficulties in making a diagnosis of valvular disease in rheumatic patients without a long period of observation has been discussed by E F Bland, T D Jones, and P D. White. 172 In their follow-up study of 1000 children with rheumatic disease over a period of ten years, they observed a disappearance of physical signs of mitral disease in 83 patients There were 26 of this group who had had a diagnosis of mitral insufficiency and about half of the number had some enlargement of the heart In 53 patients both mitral stenosis and insufficiency had been diagnosed but within the ten-year period of observation, these murmurs had became maudible and the hearts had diminished in size Considering the group as a whole, the authors stated that certain kinds of murmurs did not disappear, such as the loud diastolic type with a crescendic, presystolic roll and the loud aortic diastolic murmurs It was thought probable that many murmurs indicative of mitral insufficiency and stenosis are due to cardiac dilatation, and some of the valvular damage occurring in rheumatic infections probably leaves scars without deforming the shape of the valve

Course of the Disease—A review of a large number of children with rheumatic infections has been made by R Ash ¹⁷³ The course of the disease had been followed for at least two years in all of the total of 460 patients and the average period of observation was 7½ years. Of this group, 22 per cent had died as a result of their rheumatic in-

fections The first symptoms of the disease in 58 per cent of the number of patients were migratory arthritic pains It was interesting to note that within a period of a year or two the majority of children had forgotten their early symptoms, which suggested the difficulties of obtaining accurate past histories of rheumatic symptoms from such patients In 17 per cent of the group the carditis was the first symptom of the rheumatic disease, and chorea was the first manifestation in 21 per cent The average age at the time of the onset of the illness in these children was 76 vears

The disease was found a little less frequently in the Negro race but when it did occur it usually ran a more severe course On the other hand the rheumatic infections occurred in higher than average percentages among Italian children but the carditis was usually less In the Jewish race the death rates from this condition were relatively high Chorea, alone, appeared to cause carditis in very few instances and the prognosis of patients with this single manifestation only, was relatively good The prognosis was more serious in children who had evidence of pericarditis and pneumonia because these complications were usually associated with very severe carditis Valvular damage of the true mitral stenosis type, was usually of grave significance Cutaneous manifestations were noted in only a small group and did not seem to have much bearing on the prognosis of the disease, although erythema multiforme or annulare seemed to be associated rather frequently with severe rheumatic infections The occurrence of purpura was noted in a very small number of patients but it was questionable whether this symptom was related to the rheumatic infection Epistaxis and abdominal

pain were noted in 13 per cent of the patients and a very small group of children developed an acute hemorrhagic nephritis which later was followed by cardiac symptoms indicating valvular The death rates from rheudamage matic infections have tended to decline during the past few years and the author hoped that this was the result of more careful supervision by the clinics, although the changes may have been due to an enlargement of the groups considered, because patients with milder symptoms were being admitted to the clinic It is also possible that there are fluctuations in the severity of the rheumatic infections which follow temporary and periodic courses

A summary of the rheumatic heart disease condition in children in Chicago has been reviewed by S Gibson and E J Denenholz 174 Of their 73 patients followed with clinical and postmortem studies, only about one-fourth of the group had had a history of a cold or sore throat preceding the definite rheumatic symptoms and only about onefourth had had a history of frequent attacks of sore throat In four instances scarlet fever immediately preceded the rheumatic symptoms while growing pains were relatively infrequent complaints Chorea occurred in about one-fourth of the number of patients and about two-thirds of the children had histories of joint pains Children whose rheumatic infection began with an attack of chorea, had a better prognosis than those in which the joint pains were the first manifestation 40 per cent of this series of patients, the first attack of carditis proved fatal, which is a relatively high incidence for children Pericardial friction rubs were heard in at least one-half of the group during the course of the illness and rheumatic nodules occurred in more than

a third, although it is questioned whether more may not have had this symptom at some time at which they were not observed Auricular fibrillation developed in seven patients and of the valves. the mitral was involved the most frequently, although the aortic was affected in more than half of the group and the tricuspid in approximately the same number All but 11 of the series had evidence of pericarditis, either from clinical findings or at post-mortem examination, although the amount of fluid in the pericardial sac was always found at autopsy to be small in amount, rarely more than 200 cc

Observations of the clinical course of 750 patients with rheumatic heart disease in New York has been reported by I R Roth, C Lingg and A Whittemore 175 First observations were made at the average age of ten years and in most cases it was first made before the child was 14 years of age The average period of observation was eight years from the time of the onset of the initial Polyarthritis was the most infection common type of initial infection, occurring in 66 per cent Carditis was noted in 32 per cent, chorea in 25 per cent In only one per cent did all three manifestations occur Although the mean age of the children at the time of the onset of the first theumatic symptoms was seven years, 25 per cent had rheumatic manifestations during pre-school ages and the remaining three-fourths of the group at ages between 5 and 13 years Polvarthritis occurred earlier in life There was considerthan did chorea able evidence of recurrence of the symptoms and usually the recurrences were of the same type as the initial infection Sixty-eight per cent of the patients had at least one recurrence during the period of observation, and 74 per cent of the chorea patients had recurrences Carditis

following chorea only, was a very unusual event

The general course of rheumatic fever ın a New York clinic has been surveyed also by M G. Wilson 176 The report included the course of the illness in 225 patients who had lived to the age of 16 to 30 years and of 112 who had died during a 24-year period of observation symptoms of rheumatic activity seemed to decrease considerably after the age of 16 years and it was often difficult to obtain the regular attendance of such patients to a clinic unless there was considerable cardiac damage. The amount of cardiac damage was comparatively independent of the severity of the various rheumatic manifestations In the majority of the children who were living, the cardiac disease had progressed much more insidiously than in those who had died of the disease The average age of death was 12 years and the greatest number of deaths occurred in children between the ages of 12 and 16 years Only 13 per cent of the group were free from recurrences of the infection before the age of 16 years but 66 per cent were free from such manifestations after that period It was difficult to find any evidence which would allow one to make a definite prognosis of the child's condition and it was suggested that less reliance be placed upon anatomic cardiac findings than upon the functional ability of the heart to carry on its work The majority of patients who had shown little symptonis of carditis were those who were now alive and able to carry on ordinary work or play without circulatory disturbances Symptoms of valvular involvement changed frequently throughout the course of the patients' lives and the diagnosis of cardiac enlargement by x-ray examination, gave a better indication of cardiac damage than could be obtained from the physical examinations alone It was

the opinion of the author that the treatment or prevention of recurrences of rheumatic fever by changes in climate should be extended to cover the entire prepuberty period, if beneficial results from such methods were to be expected.

Complications — Considerable attention has been given lately to the symptom of abdominal pain associated with rheumatic infections in children. A recent review of J. B Wolffe and C J Brim¹⁷⁷ stated that the symptoms are usually of short duration, lasting from one hour to three days, and consist of fleeting attacks of nausea and vomiting which may disappear by the next meal time. Pain may begin in the upper part of the abdomen and localize in the umbilical region but it may also be generalized and not accompanied by tenderness and rigidity. The temperature may be elevated to as much as 101° F (383° C) Mild joint pains are sometimes associated with the abdominal symptoms but the latter condition can occur alone, and only the continued observation of the cardiac condition will lead to the correct diagnosis of rheumatic fever Occasionally the appendix becomes inflamed in the early stages of rheumatic infection and produces abdominal symptoms of a similar nature Operative treatment is necessary in such patients

Appendicutes in patients with rheumatic fever has been discussed recently by A T Martin and S L Ellenberg ¹⁷⁸ They call attention to the difficulties involved in differentiating appendicutes of rheumatic origin from that of other causes. The abdominal symptoms frequently precede the other manifestations of rheumatic fever, but if the patient has had a history of previous rheumatic attacks, a short period of observation, not longer than 24 hours, was considered justifiable. During this time, salicylate therapy may be tried but if relief is not

obtained, operative procedures are necessary regardless of the etiology of the appendiceal inflammation

The frequency with which pericarditis occurs in patients with rheumatic fever has made it important to employ every clinical facility for diagnosing the condition Rheumatic infections of low grade activity may be detected by the discovery of signs of pericardial inflammation J B Wolffe and V A Digilio¹⁷⁹ call attention to the friction-like, almost musical murmurs which are best heard in the left second and third interspaces near the sternum but are occasionally audible at the apex These sounds are usually systolic in time, but may be diastolic or combined to cause "to and fro" murmurs These murmurs may be transitory but they do not disappear on deep breathing and are accentuated by placing the patient in a prone position. It seemed probable to the authors that the sulcus between the aorta and pulmonary artery was a locality often invaded by inflammatory processes in rheumatic carditis

An unusual complication of rheumatic fever is meningitis Such a patient was reported by G Bourne 180 The patient, aged 34 years, developed a typical attack of polyarthritis and 12 days later had neck rigidity and a positive Kernig's sign The spinal fluid was somewhat turbid, under increased pressure and contained red blood cells and leukocytes. Although this may have been an intercurrent affection, such as encephalitis, or cerebral hemorrhage the author believed that the meningeal symptoms in this case were related to the rheumatic infection The patient made an uneventful recovery

Treatment—Repeated blood transfusions have been employed with some success in the treatment of patients with rheumatic fever. Recently this form of therapy was tried by L. C. Rosenberg¹⁸¹ in a boy nine years of age who had had

repeated attacks of that disease A fall in the erythrocyte sedimentation rate and a slow drop in fever followed several transfusions The mechanism of the treatment is not known but it seemed to help combat the anemia and to supply some antibodies which aided recovery. It was suggested that further trial be given to this type of treatment

A close relationship between the bacteria and toxins of rheumatic infections and scarlet fever has been claimed by numerous investigators and has led to a trial of antiscarlet fever serum as a therapeutic agent in rheumatic disease In a patient observed by J Eason and G Carpenter, 182 massive salicylate therapy failed to relieve rheumatic symptoms but the administration of antiscarlatinal serum brought about a rapid subsidence This led the authors to give the treatment a more thorough trial in a group of 44 rheumatic patients, mostly adults The incidence of relapses was reduced, the stay in the hospital and general progress of the illness seemed to compare favorably with results obtained from salicylates alone The outstanding disadvantages of the serum were the reactions which it produced in a number of the group and the rather high prolonged fever resulting from its administration. Whether the antiscarlatinal serum acted as a specific antibody for the rheumatic infection or as a general foreign protein only, is still open to question

Chorea

Considerable doubt has arisen within the past two or three years as to the importance of chorea as a manifestation of the rheumatic syndrome. It is the opinion of some that this disease is not of the same etiology as rheumatic fever although the latter disease may be one of many conditions which predisposes to the chorea. This is the opinion of A. F.

Coburn and L V Moore, 183 who have reviewed their experience with chorea during the past year In about 30 per cent of a group of 114 patients, chorea was the only condition noted and no other rheumatic activity occurred another group of 137 patients with chorea, about half had no rheumatic manifestations The blood sedimentation rates and leukocyte counts in such patients were usually normal If these two groups may be taken as samples of the population of that district, one might say that about one-half of all the cases of chorea in New York were free from rheumatic fever The remaining half of the group had chorea in association with quiescent rheumatic infections in about 50 per cent of instances and during active rheumatic infections in the other 50 per cent of cases

Treatment—The treatment of chorea by raising the patient's body temperature has given good results in the hands of C A Neymann, M L Blatt and S L Osborne 184 They employed electromagnetic induction methods and raised the children's temperatures to 105° F $\,$ (40 5° C) or less Twenty-five children treated in this manner with an average of four treatments, improved after an average stay in the hospital of 16 days The most severe attack of chorea required ten biweekly treatments and the choreiform movements did not subside for 39 days Observation of the patients for a period of 1 to 20 months revealed that only three had recurrences (12 per cent of the Cardiac disease seemed to be group) no contraindication of treatment and the only complications observed were herpes labialis, and one instance of transitory albuminuria and hematuria One patient developed convulsions probably as the result of too elevated a temperatureabove 105° F (405° C) Of a group of 31 other chorea patients who have

been treated by other clinicians with external heat produced by other methods, 28 were reported to have been improved and six had recurrences

The administration of typhoid vaccine to chorea patients to produce fever has been criticized in the past because of the severity of the reactions it produces in the patients. Recently, however, encouraging results have been reported by D Weisman and C Leslie 185 They employed a concentrated vaccine prepared by the New York City health department and injected it intravenously in initial doses of 0.05 cc. The temperature reactions and the clinical course of the patient determined subsequent dosage and the number of injections Fevers of 104° to 107° F (40° to 416° C) were obtained in most cases without any danger to the patient and without impairing his general health. Daily injections with increased dosage often had to be employed to produce these fever reactions The average number of injections required was eight or nine with ranges between 2 and 22 Fifty patients with chorea made up the experimental group, and 38 of these had severe attacks, four violent ones and eight were only mildly The results in general, as affected judged from the duration of the disease and the relief from symptoms seemed to compare very favorably with other forms of therapy and to be free from danger, even for patients with carditis Careful observation of the patients by nurses and physicians is necessary during the period of treatment

Endocarditis

Acute Bacterial Endocarditis — In their report of a boy, four months of age, with acute bacterial endocarditis, F W Mulsow and H R Hess¹⁸⁶ stated that no evidence of cardiac murmurs could be determined clinically. The physical

examination of the patient was entirely negative except for the discovery of petechiae beneath the toe and finger nails several days after his admission to the hospital The pulse was very rapid and the temperature high A hemolytic strain of streptococcus was isolated from the blood stream and the throat was apparently the portal of entry The patient died 17 days after the onset of his illness and at autopsy, vegetations were found on the aortic valve Only five instances of acute bacterial endocarditis in infants less than seven months of age have been described previously in the medical literature

Two instances of endocarditis in very young infants have been observed by E S Giddings 187 One infant, two months of age, developed lesions on the aortic valve, caused by a streptococcus viridans. The other patient, four days of age, had vegetations on all the heart valves as a result of a pneumococcic infection. In neither patient was there an indication of infection of the mother.

Electrocardiography in Children

Of considerable importance in the interpretation of electrocardiograms of children is an understanding of the variations of the tracings obtained from normal patients. The electrocardiograms of 100 normal children have been reviewed by F M Hafkesbring, C E Drawe and R. Ashman 188 The mean age of these children was about nine years with ranges from infancy to 14 years, and the group was composed of both sexes and included 28 patients of the negro race The average duration of the P wave was 0 062 seconds with an upper limit of 009 seconds. The upper limit of the height of the P wave in Lead I was considered to be 15 mm and in Lead II, 25 mm Inversion or a diphasic type of the P wave in Lead III occasionally oc-

curred, and a notching was seen in isolated instances, but not consistently throughout a tracing. The duration of the P-R interval was considered to be 0.132 seconds as an average. Variations did not occur with sex but the duration was longer in older children and in hearts with slower rates.

The QRS complex averaged 0065 seconds in duration with the upper limits 0.09 seconds Increases in duration accompanied increasing age of the patients Low voltage or slurring of the QRS wave or variations in the height of the R wave rarely occurred in these normal children and only slight deviations of the axis to the right or left were noted The RS-T segments occasionally had an upward shift and the T waves were high, with boys exhibiting higher T waves than the girls, as a rule The T wave in Lead III was frequently inverted or diphasic but no notching occurred Premature ventricular beats occurred in only one of the normal patients

The electrocardiographic findings in 100 children with rheumatic heart discase were compared with tracings of 100 normal children of approximately the same age distribution by C E Drawe, E M Hafkesbring and R Ashman 189 The cardiac lesions of the 100 rheumatic fever patients consisted in various degices of mitral insufficiency or stenosis and aortic regurgitation or combinations of these defects As a rule, the cardiac rates were more rapid in the rheumatic group, the P waves were more conspicuously notched, widened and elevated, and the P-R intervals were prolonged The QRS waves were generally normal except for a slight prolongation and occasional notching. The axis deviation tended slightly towards the right in patients with mitral disease and to the left in patients with aortic lesions Abnormalities of the T waves consisted of low voltage, diphasic characteristics in Lead I and rounded, notched or inverted types in Lead II The Q-T interval was prolonged in most rheumatic patients. Some tracings of rheumatic patients in this group were entirely normal

The same authors (loc cit) analyzed the electrocardiographic records of 50 children with congenital heart disease and compared the findings with tracings of normal children The congenital heart lesions consisted of various degrees of pulmonary stenosis, including some with the tetralogy of Fallot, interventricular defects and patency of the ductus arteriosus The P waves in the group of patients with pulmonary stenosis were greatly increased in height and width and the QRS waves in the same group were longer than average P-R intervals in the entire group of congenital heart patients were about normal but the QRS complexes were generally of greater duration and frequently notched or slurred, especially in the patients with pulmonary stenosis All children with this diagnosis showed right axis deviation. The T waves of all of the group were generally higher and frequently inverted in Leads II and III

Electrocardiographic findings in congenital heart disease are of greatest importance in certain cases of dextrocardia, congenital heart block or other disturbances of conduction but in a recent study of 43 cases of congenital heart disease, L N Katz and H Wachtel¹⁹⁰ found certain changes in the QRS complex which they believed were typical of congenital heart disease in general There was a tendency for this complex to be diphasic with the smaller phase having an amplitude of at least one-fourth of that of the larger phase In 56 instances of a total of 129, these diphasic QRS complexes were noted, most frequently in Lead I and least frequently in Lead II. Cases in which the positive or upright phase was the more prominent, were the most common. There was a tendency for the upright phase to be prominent in more than one lead in about half of the number of this series, and to be upright in one lead and downward in another in the same number of patients The ORS complexes in general tended to have a large amplitude and slurring occurred in 13 patients Other findings included right axis deviation in 16. left axis deviation in five, but abnormalities of the T wave and S-T segment were relatively uncommon Many of these changes seemed to occur in the electrocardiograms of these patients regardless of the type of cardiac lesions which they represented.

The significance of the fourth lead tracings of normal children and of those with rheumatic heart disease has been studied recently by M Robinow, L N Katz, and A Bohning 191 The T waves in the fourth lead tracings of normal children varied from time to time and were observed to be upright, diphasic or polyphasic Acute rheumatic fever frequently resulted in the production of upright T waves in a greater majority of instances and these waves often became negative as the patient improved Lead IV did not seem to give much more information than the three conventional leads and sometimes they were unreliable. To be of any value it seemed to be necessary to take a series of such tracings to determine definite trends of the changes and variations

Little additional information could be obtained from Lead IV by C R Messeloff and A Pomerantz¹⁹² in a study of the tracings of children with rheumatic heart disease In a series of 141 children in various stages of activity of

their rheumatic infections, the waves in the fourth lead showed considerable variation in form and direction. These characteristics may occasionally be observed also in children with normal hearts so that the authors were convinced that the three conventional leads gave all the possible information which could be obtained by electrocardiography in children

MEASLES

By Waldo E Nelson, AB, MD

INFANT FEEDING

M L Blatt and H Kessler¹⁹³ believe that unboiled breast milk has distinct advantages over that of boiled breast milk for the feeding of infants, especially premature infants This advantage, they believe, is due to the lysozyme and the indigenous bacteria which are destroyed by boiling In their experience, raw milk with a bacterial count of less than 10,000 per cubic centimeters which has been obtained manually under aseptic precautions from women free from tuberculosis, syphilis and acute infection, and having normal breasts may be pooled and kept in a refrigerator for from 24 to 72 hours and may be safely fed to premature and young infants

Gelatinized Mılk

C L Joshn¹⁹⁴ has had better success in the feeding of infants if either gelatin or acid is added to cow's milk formulas than with immodified cow's milk formulas. A better rate of gain was noted for both of these low curd tension milks and vomiting and constipation appeared to be reduced. In addition, a smaller percentage of infants developed diarrhea on the modified milk than on the unaltered cow's milk It was noted that two per cent gelatin was definitely more effective in overcoming constipation and vomiting than was one per cent In making the gelatinized milk, gelatin is added, one or two per cent, by placing the necessary amount of gelatin in the amount of water to be used in the formula The water should be boiled and allowed to cool at room temperature before the gelatin is added. This mixture is then allowed to stand for ten minutes before being added to the milk

MEASLES

Further investigation of the nature of placental extract and its effect in the prevention and modification of measles has been reported. The effectiveness of this material compares favorably with results obtained with the use of human convalescent serum. Oral administration does not appear to be as satisfactory as the subcutaneous or intramuscular routes. It is thought that further refinement of the placental extract might eliminate proteins causing local reactions in patients.

Complications — Encephalitis occurring as a complication of measles has been reported with increasing frequency lately. Various clinical types of the complication have been observed, depending upon the portion of the brain primarily involved. In the five patients reported by G. A. E. Barnes, J. C. Blake, J. C. Hogarth and M. Mitman¹⁹⁵ the sphincter of the bladder was involved in all, meningeal irritation signs occurred in two and mental disturbances with disturbed consciousness in three. Treatment included the use of such drugs as

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glucose, hexamine or sodium salicylate given by mouth or intravenously, magnesium sulfate by all routes, and human convalescent measles serum introduced into the muscles or the blood stream and occasionally into the cerebrospinal canal. The authors observed an especially good response to the intravenous administration of convalescent serum in one of their patients.

The occurrence of measles encephalitis in Canada has been rare H W Price¹⁹⁸ was able to find reports of only two previous cases in that country and he added three of his own experiences with the disease in children seven months, four years and five years of age, respectively, who had been seen over a period of years from 1932 to 1935 The youngest patient died of the disease and the others made complete recoveries An interesting observation was that two patients, who developed encephalitis following exposure to measles, never had any evidence of the rash

Encephalitis as a complication of measles had been noted in a patient who had suffered from a meningitic complication of mumps during the previous year M L Bridgeman¹⁹⁷ reported that a secondary rise in fever and symptoms of restlessness, delirium, and irregularity of respiration occurred five days after the appearance of the measles rash The cerebrospinal fluid was normal and the patient made a complete recovery The author wondered whether there was some characteristic of individuals which caused them to react with nervous symptoms after such diseases as mumps and measles

A "inyelitic" form of involvement of the central nervous system following measles was observed in a boy, eight years of age, by C Rosenheck and H Barowsky ¹⁹⁸ Nine days after the onset of measles, the patient developed a sec-

ondary rise in fever, pain in the back, abdomen and legs, and loss of motor power in both legs. The tendon reflexes of the legs, and abdominal reflexes were absent and marked hyperesthesia developed in the lower limbs. Within a few months the boy recovered completely except for a slight alteration of his gait in walking.

The influence of measles in activating tuberculous infections is one of the worst sequelae of that disease Added proof of such relationship has been given by P. Svastits¹⁹⁹ who observed 70 children with positive tuberculin reactions who were recovering from measles By means of roentgenograms, he noticed that seven or ten per cent of the group had evidence of a flare-up of the pulmonary tuberculous lesions He urged that all small children and those with positive tuberculin reactions be protected from measles, or the course of their disease modified, by the administration of such materials as convalescent serum or immune adult serum

A similar study of the effects of measles on tuberculosis was made by N Carrara 200 Among a group of 1470 children, 112 per cent had evidence of some effect of the measles infection upon tuberculosis Under the age of five years, children were more prone to show a lighting-up of tuberculous foci than in older age groups Measles was especially dangerous in younger children with recently acquired tuberculous infections, and measles was found to be especially disastrous when it developed in anyone who had active tuberculous lesions regardless of the age of the patient For a period of at least a year, measles seemed to exert an influence on the course of tuberculous infections

Nine instances of appendicitis occurring early in the course of measles have been observed by H W Hudson, Jr,

and C Krakower 201 The symptoms of appendicitis occurred on the day of the development of the exanthem in three patients, on the fourth to seventh day after the rash in four patients and one to three days before the rash in the other two children. The question of the part played by the measles virus in causing the appendicitis is still undecided, but the pathologic examination of the appendices of the author's series demonstrated a diminution of lymphoid tissue with a lack of germinal centers and an increase in the number of plasma cells in the mucosa, in contrast to the findings which usually occur in such tissues of children who contract other types of acute appendiceal infections

About 31 cases of measles and appendicitis have been described previously in the literature and the concensus of opinion is in favor of operation if signs and symptoms of appendicitis appear, in spite of the presence of measles (See Appendicitis, page 932)

An unusual complication of measles, the development of cancrum oris, has been described recently by L H Mac-Farlane 202 Thirteen days after an attack of measles a boy three years of age developed a necrotic area on the inside of the lower lip. The temperature rose to 103° F (395° C) and the lesion became gradually worse, spreading out over the left cheek, accompanied by edema over the left side of the face. neck and upper chest wall. The area became purple, broke down, and a thin fluid escaped Six days later a large slough occurred at the angle of the mouth and the patient died The etiology of this condition could not be definitely deternined since the organisms recovered from the lesion were mixed in type. There was no evidence of an agranulocytosis and the patient failed to respond to the administration of anti-diphtheria or anti-scarlet fever serum.

Prevention-Favorable results with the use of *ımmune globulın* derived from placental extracts continue to be reported in the medical literature The material is used as one would employ human convalescent serum or immune adult serum for giving a child a passive immunity to measles of a few weeks duration or of providing an attenuated attack of the disease if it is given to an exposed child early in the incubation period of the disease Satisfactory results in ameliorating measles attacks from the administration of immune globulin to 49 children exposed to measles in an institution have been reported by H Goldstein, H M Eisenoff and S A Blauner 203 A total number of 128 children between the ages of $1\frac{1}{2}$ and 10 years were exposed and a group of 49 were selected to receive immune globulin injections, 27 of them within the five day period after exposure. In the other group of 79 children who received no treatment, the incidence of measles was higher, the attacks were more severe and the complications were more frequent than in the group of treated children

Placental extracts have been found effective in protecting children against measles if given early enough in the incubation period U Moeller²⁰⁴ administered 10 to 15 cc to 47 exposed children and only three per cent of the group contracted the illness Of a series of 44 children receiving 3 to 20 cc of the extract on the fifth to seventh day of their incubation periods, only 20 per cent were entirely protected

Since the potency of placental extract, like that of human convalescent serum, differs considerably, S Karelitz, C K Greenwald and A. J Klein²⁰⁵ have devised a method for the determination of

by cutting and squeezing of human placentas to express the fluid and blood, centrifuging the liquid and using the supernatant fluid, which was then treated with merthiolate, dialyzed, the pH adjusted to 68 and then filtered through a Berkefeld filter Experiments with the placental extracts prepared in this manner have demonstrated that the diphtheria antitoxin content is the same in the placental fluid as in the paternal blood of the mother at the time of delivery of her baby.

tered in varying dosage to 64 infants exposed intimately to measles, it was found to contain antibodies against measles in quantities similar to that of immune adult serum. Rather than use the nitrogen content of the placental extract as the basis of determining the concentration, the authors employed the test of its diphtheria antitoxin Having judged the potency of the extract, they employed a formula which allowed the dosage to be adapted to the amount of immune adult serum which would ordinarily be employed

MENTAL DEFICIENCY IN CHILDREN

By ROBERT A LYON, AB, MD

Mongolian Idiocy

Three interesting phases of mongolism have been observed by W J Johnson ²⁰⁶ In one instance, mongolism occurred in a patient whose twin brother was a mental defective and later developed dementia praecox of the paranoid type. In another family of the negro race, mongolism occurred twice, in children of the fifth and ninth pregnancy. A third family of Russian parents had in succession two children with the physical characteristics of mongolian idiocy.

Although mongolian idiocy seems to occur in all races, no report of it in the American Indian was recorded until that of J Sirkin ²⁰⁷ He has observed three such patients in Indians at the Newark State School

The occurrence of Mongolism in twins is of considerable genetic interest. The condition has been observed previously in one of a pair of non-identical twins but in a recent report by L. MacKaye²⁰⁸ mongolism was present in both of a pair of non-identical twins. It led the author to doubt the occurrence of a regressive

mutation as the cause of the condition and to give greater importance to certain environmental factors. Although no definite etiology of mongolism has been determined, the age of the mother apparently bears the most definite relation to the occurrence of this type of idiocy

Familial Cerebral Sclerosis

This condition in two infants of the same family has been recorded by D S Russell and K H Tallerman 209 The parents of these children were Jewish and cousins of each other The symptoms of cerebral involvement developed a few weeks after birth and resembled those usually associated with cerebral injury or hemorrhage One child died at the age of five weeks and the second child died when it was six months of age. At the autopsy of the second patient, there was found a degeneration scattered throughout the white matter of the cerebrum and cerebellum, and the involvement of the cortex The sulci of the cortex contained much more evidence of tissue change than the tops of the convolutions and

almost none of the lesions were of a distinct inflammatory nature and there was no proliferation of the blood vessels. The microscopic sections showed a demyelination and a marked reaction of the glial tissues, but no lipoid tissue was present. The etiology was undetermined

Hydrocephalus

The value of roentgenology in the diagnosis of hydrocephalus has been reviewed by M B Kopylov 210 The size, shape and configuration of the skull, the thickness of the bones and the relations of one part to another have a certain diagnostic value In the so-called "open forms" of hydrocephalus, due to hypersecretion or to failure of resorption of the fluid without impairment of its circulation throughout the central nervous system, the sella turcica does not vary much in form The closed types of hydrocephalus in which the fluid is trapped in one portion of the brain seemed to produce certain deformities in the basilar bone structures. The author has stated that one may even localize the position of the block in certain cases by the study of the structural form of the sella turcica

Two patients with chronic hydrocephalus and signs of sexual precocity were observed by G B Dorff and L M Shapiro ²¹¹ The postmortem examination of one patient showed normal glands of internal secretion except for a compression of the pituitary as the result of a continued increase of intracranial pressure. The ovaries contained many follicular cysts. It was believed that a relationship between lesions involving the hypothalamic infundibular-hypophysial pathway and precocious sexual development was possible.

Internal Hydrocephalus—This unusual condition, resulting from the thrombasis of the cerebral sinuses, was re-

ported by R W B Ellis ²¹² It occurred in an infant, five months of age, who had multiple areas of thrombosis probably the result of sepsis originating in the infected umbilical stump, although the infant also had a respiratory infection which might have contributed to the septicemia. The thrombosis in the cerebral sinuses led to hemorrhage within the skull and subsequent obstruction to the flow of cerebrospinal fluid.

Lawrence-Moon-Biedl Syndrome

The group of symptoms classified as the Lawrence-Moon-Biedl syndrome includes obesity, hypogenitalism, retinitis pigmentosa, mental deficiency and polydactylism Many variations of this syndrome have been reported in which only a portion of the above symptoms occur but sometimes with added findings of congenital heart disease, strabismus or deformities of the skull A review of such case histories has been made by J Warkanv, G S Frauenberger and A Graeme Mitchell²¹³ together with a report of four instances of incomplete forms of the disease Only 14 of the 102 previously reported patients have had the exact combination of defects required by the Lawrence-Moon-Biedl syndrome and it was the conclusion of the authors that such a classification was unjustified Many degenerative types of lesions may occur in all soits of combinations and to group any few together as a specific syndrome clouded the general aspects of the picture

Considerable attention has been paid in recent years to the relation between hypoglycemia and the convulsions which occur in many mental defectives. Such convulsive attacks are often preceded by fatigue, malaise, hunger and confused speech. In testing 50 cases of convulsions in children, aged 2 days to 11 years, with such conditions as birth injury,

spasmophilia, meningitis, epilepsy and acute infections, M B. MacLean²¹⁴ found an initial rise in the blood sugar for a few hours after the convulsion and then a hypoglycemia which lasted from several hours to several days The author believed that these disturbances of the blood sugar levels were the result of the convulsions rather than the cause of the symptom The hyperglycemia which occurred in about half of the group of children following convulsions seemed to be due to excessive secretions of adrenalin and the subsequent fall in blood sugar levels may have been the result of an exhaustion of the adrenals or related internal secreting glands. In two instances the administration of adrenalin was followed by a rise in the blood sugar level. It was the conclusion of the author that convulsions were rarely the result of disturbances of carbohydrate metabolism except in instances of hyperinsulmism

Treatment and Education of Mentally Defective Children—The methods and facilities employed in the state of Ohio for the education of mentally retarded children has been summarized by C S Berry ²¹⁵ Since the school system is responsible for the child of school age until he has reached the age of 18 years, regardless of whether the child is able to do the school work, provision for education or supervision is necessary throughout this entire period of time

Some children with very low mental capacity who are unable to profit at all from education may be sent to a state institution for the feeble-minded, but the large proportion of such patients continue in the schools. Since the subject matter in school curricula is impossible for the mentally deficient child to grasp, it is necessary to provide the special types of training, which emphasize habit

training and imitation In the larger cities special classes for mentally retarded children have been instituted which have the advantages of specially trained teachers, special subject matter and facilities for the development of the retarded child Disadvantages arising from this arrangement are the increasing costs and the opposition of parents who realize that their child is segregated from the group as a whole Such children have less opportunity to compete or to associate with the normal child in activities such as sports, games and manual activities of all types in which he can be as successful as the normal child In the smaller communities it is possible to arrange the special class within a school and provide a single teacher for such instruction who might be especially interested in that type of work or who has received training for such teaching, but such a class has the disadvantages of including children of various age groups and of various stages of training A third possibility is modified individual training whereby the mentally deficient child is passed along with the grade in which he started but is given modified types of work which are adapted to his capabilities This requires the least specialized type of instruction, although it provides less satisfaction to the pupil in many instances because he is unable to occomplish his tasks and to keep up with his friends However, it is often very satisfactory in the small community and is approved by parents The author stressed the importance of providing, when possible, sufficient equipment and sufficiently trained teachers to adapt children to vocations in which they may be satisfied It is important to follow these patients during the years after their school work has ceased in order to insure their proper adjustment in the world The parents and the community must

be taught to understand the mental deficient and to provide facilities whereby the defective child may gain a livelihood and adjust himself in his environment

The importance of supervising mentally inferior children during the first few years of their lives after leaving school, especially when they have entered occupations, has been stressed also by M Keator ²¹⁶ During the last few years efforts have been made in Hartford, Connecticut, to follow the children between the ages of 16 and 21 years in an attempt to teach them to persist at the jobs which they have undertaken and to elicit the cooperation of the family and

of the employer in efforts to keep the child at his work. The results were encouraging in a large number of cases in which mentally inferior youths were able to earn small amounts of money and thereby keep off the relief rolls Only a small amount of supervision was necessary for this service and the money expended was but little in comparison with that which was saved by the community In most cities it is difficult for children of this age to obtain employment so that the training of the mental defective for his 10b and the efforts to make the 10b attractive for him are items of considerable importance

MUMPS

By Robert A Lyon, AB, AM, MD

One attack of mumps usually confers lite-long immunity to a patient although unilateral parotitis may be followed after a period of years by an attack of mumps on the opposite side. More rare is recurring parotitis such as C R Brown and W B Nevius²¹⁷ observed in a voung boy of five years. Attacks began at the age of three months and occurred at intervals of every three or four months thereafter Not until the age of six years did the child develop orchitis and at that time mumps and orchitis were contracted by the father, apparently from his exposure to the child The attacks of parotid swelling seemed to follow upper respiratory infections and were terminated by removal of the tonsils and adenoids

Unusual complications of mumps, which have been reported recently, include two instances of ocular paralysis observed by T H Butler and A J. Wilson ²¹⁸ In both cases, disturbances of vision and regurgitation of food

through the nose had occurred from one to three weeks after attacks of mumps One child, aged nine years, had a paralysis of the muscles of accommodation and of the pupillary reaction to light. The optic discs were blurred. Observed again after a period of four years, the boy was found to have recovered completely. In the other patient, who was 12 years of age, the third nerve on the left side was involved, which resulted in a ptosis of the left lid, and the pupil on that side was inactive. Only slight improvement occurred during the following month of observation.

Meningeal irritation during the course of mumps occurs with considerable frequency but an instance of unusual severity has been noted in a boy six years of age by M L Bridgeman ²¹⁹ Symptoms of fever, severe pain in the legs and knees, irritability, restlessness and stiffness of the neck occurred several days after the parotid swelling. The cerebrospinal fluid contained 119 cells at the

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height of the illness and the patient made a complete recovery within nine days after the symptoms of the complication were first noted.

Treatment—The use of human convalescent serum in the treatment of mumps has been given a trial recently when a severe epidemic of the disease broke out in a school of young adults R G Hinckley²²⁰ administered the serum to 23 who contracted the illness in the latter part of an epidemic The course of

their illness seemed less severe and was followed by fewer complications than was the case in the group of 55 untreated boys who had contracted the illness during the first part of the epidemic

An interesting observation by the authors was the relatively large number of patients (32 per cent) who developed glycosuria during the disease. It was noted more frequently among the patients who had severe infections and among those who received the serum therapy

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By ROBERT A LYON, AB, AM, MD

Diseases of the Newborn

Tying the *umbilical cord* immediately after birth instead of waiting until pulsation ceases seems to favor a lowered incidence of *jaundice*, possibly preventing the occurrence of a polycythemia or increased fragility of these cells

The most satisfactory treatment of *icterus gravis* continues to be *blood transfusions* and injections of *dextrose* solutions

The *etiology* of tetany in the newborn has been ascribed to hyperventilation and the treatment has consisted of the administration of carbon dioxide and oxygen

The most common cause of cyanosis in the newborn, according to Morgan and Brown, is the aspiration of mucus, which is most satisfactorily removed by suction of moderate force although McGrath and Kuder recommend the introduction of a tube into the larynx of the infant by direct laryngoscopy, removal of mucus and other fluids by suction and insufflation of a mixture containing 90 to 95 per cent of oxygen and flive to ten per cent of carbon dioxide.

Prematurity

Great variations occur in mortality rates among premature infants reported by hospitals of different parts of the country E C Dunham²²¹ has stated that the rates varied from 18 to 94 per cent in more than 100 hospitals in 27 large cities of the United States These figures lack uniformity in the material covered and the sources from which they are derived They represent premature infants born in hospitals only or include those sent into institutions The birth weight from the outside classification dividing the premature infants from mature infants is an arbitrary matter and differs in various localities Death rates of premature infants vary with the length of observation period Although the mortality rates of all infants under one year of age have declined during the past 18 years, the deaths from prematurity have not decreased at anything like the same rate so that prematurity is now one of the chief causes of post-natal death Four or five per cent of every 100 deliveries are premature infants although some statis-

tics find the percentage as high as six or seven. Factors causing prematurity have never been determined accurately although it has been assumed that the chief causes are multiple pregnancies, toxemias of pregnancy and abnormalities of the placental position Causes of death of prematures have not been adequately established, but pathologic reports have indicated that intracranial hemorrhage, septicemia, asphyxia, atelectasis, play a considerable part in the death of these children Many attempts have been made to reduce the mortality of premature infants by providing a satisfactory environment of elevated temperature and humidity, the isolation of the infant from infection, prevention of the early delivery by the roentgen ray examination of the fetus within the pelvis, and the general education of physicians and the public in methods of caring for this type of child The author stresses the need for more statistics of a definite nature in regard to events responsible for premature delivery, the methods of care and treatment and the general dissemination of such knowledge as we have which might reduce the mortality in this age group

When the mortality rates of premature infants are computed with an exclusion of the deaths occurring in the first 48 hours figures as low as three per cent have been obtained. In the review of the subject, made by W. W. Swanson, E Lennarson and F L Adair, 222 which included a group of 752 premature infants who had been born during the course of 10,660 consecutive births, the total mortality rate was 178 per cent but the elimination of the deaths occurring within the first 48 hours reduced the mortality to less than three per cent The primary causes of death in this group of prematures were congenital weakness, accidents of labor, malforma-

tions of the infants and asphyxia Syphilis, pneumonia and gastrointestinal disturbances did not play a prominent part in the death of these patients. The infants of very small weight tended to regain their birth weight as rapidly as did those who were heavier and nearer In the treatment of this group of patients, all of which were born within the hospital, a box type of incubator with a 40 watt lamp was used to maintain the heat of the infants The feedings were relatively simple, consisting chiefly of breast milk or a formula composed of two-thirds cow's milk, one-third water and five per cent of dextrin The feedings were small and frequent but varyied with the weight of the infant Occasionally the caloric values and the mineral or protein content of the feedings had to be increased by the addition of Dryco, buttermilk or skimmed lactic acid milk

In a survey of infant mortality in the city of Chicago over a 10-year period between the years 1925 to 1935, premature deaths were found to constitute a large percentage H N Bundesen O A Dahms, W I Fishbein and G E Harmon²²³ reported a general decline in infant deaths in all age groups and a decline in the number of still births Premature births occurred in 377 per thousand live births during 1935 and deaths of premature infants constituted 58 4 per cent of the total number of deaths of infants under 30 days of age. In ascertaining factors which influenced the occurrence of prematurity, it was found that about 50 per cent of the mothers had received prenatal care and about five per cent of them had positive serologic tests for syphilis Breech deliveries were more frequent in premature infants but operative procedures requiring the use of forceps were not more frequent than in normal infants The authors found

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that toxic and pathologic conditions of the mother, the improper use of anesthetics and drugs during delivery occurred in high percentages of the premature deliveries. They urged adequate prematal care and proper facilities for the care of such mothers and their infants, as important methods of effecting a reduction of infant mortality from prematurity

An investigation of the factors which might have led to the premature birth of 244 infants has been made recently by E. C. Dunham and P F McAlenney, Jr_224 This series of prematures included only those infants who weighed less than 2500 Gm at birth The mortality rates were 100 per cent in those weighing less than 1000 Gm, 62 per cent in those weighing less than 1500 and more than 1000 Gm, 22 per cent in those weighing 1500 to 2000 Gm, and only six per cent in those weighing more than 2000 Gm The total number of deaths was 66 and more than half of them occurred within 24 hours after burth Death rates were lower in prematures resulting from multiple pregnancies than in singly born infants The mortality among ward patients and infants of private physicians was practically the same and the care given each group was identical From the investigation of the causes which may have led to the deaths, the authors were unable to find any influence of the birth order of the infant, since the offspring of multiparous and primiparous women died in the same percentages The mortality rates were the same in the group of infants whose mothers had complications as in those who had no complications The duration of labor did not influence the premature mortality rates significantly, although induced labor was followed by somewhat higher infant mortality than was spontaneous labor

Factors such as abnormalities of the pelvis and operative delivery did not seem to increase the mortality rates among premature infants. The chief causes of death among the prematures in order of frequency were prematurity, infections, intracranial hemorrhage and congenital defects. At electasis occurred in about half of the number of infants who died and delays of respiration and deaths occurred more frequently in the infants whose mothers had received morphine during delivery.

The care and treatment of a group of 330 premature infants has been reviewed recently by D A Wilcox 225 infants constituted 3.24 per cent of over 10.000 consecutive deliveries in the Sloan Hospital for Women in New York during a five-year period Prematurity was defined according to the weight of the infant (2500 Gm or less) rather than the period of gestation which was always difficult to determine The correlation between the period of gestation and the length and height of infants was found to be low The length of an infant is generally thought to be a better indication of maturity than weight but the determination of length is a much more difficult measurement to obtain accurately than the weight Treatment of the premature infants was provided in a special room in which the temperature was kept at 80° F (267° C) patients who weighed less than $4\frac{1}{2}$ pounds (2050 Gm) or having rectal temperatures of 96° F (35 5° C) or less were placed in Morgenthaler cribs equipped with separate heating devises maintaining the atmosphere at 85 to 90° F (29 5 to 32 2° C) and the humidity between 55 to 60 per cent

Feedings, begun after the infant was 12 hours old, and given at three-hour intervals, consisted of *breast milk* in quantities of 5 to 15 cc at first and in

increasing amounts per feeding until 130 to 160 calories per kilogram of body weight were offered during a 24-hour period Infants weighing less than 31/3 pounds (1500 Gm) received their food by means of gavage, the heavier ones by bottle. When the mother's milk was inadequate, the feedings were frequently supplemented after the tenth day, or replaced entirely, by evaporated milk formulas. It was the general impression of the authors that the group of infants who continued to receive breast milk had lower mortality rates than the groups dependent upon artificial feedings. Vitamins C and D, and iron preparations were administered regularly after the third or fourth week of life The mortality rate of the group during the first 72 hours of life was 4.4 per cent, during the complete hospital stay, 25 1 per cent, and for the entire period of observation, 28 5 per cent The rates for the boys was higher than for the girls in all weight groups and the most common causes of death of both sexes were prematurity itself, birth injury in the smaller infants and infection in the heavier ones. The rate of growth of the smaller premature infants was slower than that of the heavier ones but they all generally attained average weights of normal children by the time they reached six months of age

The effect of prematurity on the subsequent health of the child has been discussed by H Siedentopf 226. Of a series of 1012 premature infants born in 1920 to 1923, 100 were examined 10 to 14 years later and less detailed information was obtained from an additional group of 88. Physical and mental defects did not occur in greater proportions in these prematurely born children than in other children born at full term and the author concluded that any premature infant who survived ten years of life might be expected to compare very favorably

with the average normal child in nutrition, development and general health

A recent observation that oestrin secreted by the mother during pregnancy was most plentiful during the last months of gestation, has led some investigators to wonder whether prematurely born infants might not have suffered from a lack of this substance because of their early birth To test this point, oestrin was administered orally to a small group of premature babies by M F Potter 227 An equivalent to 500 international units in the form of progynon was given twice daily to 11 infants and their progress seemed to be improved above the average expectation One premature, sick with gastroenteritis and severe toxemia seemed to benefit from the medication

The characteristics and treatment of anaiomas in premature infants have been reviewed by A C Rambar 228 The incidence of angiomas among 344 premature white infants was found to be about 12 per cent while none were observed in 78 premature negro infants observed during the same period of time The great majority of the lesions were simple angiomas or the so-called strawberry marks Four of the group had cavernous angiomas and one had a nevus flammeus or "port wine" stain Generally these lesions were not noted at birth but made their appearance between the first week and second month of life and they occasionally occurred in multiple forms, one infant having as many as seven Various parts of the body were affected, in about 43 per cent of cases, it was the thorax, back, abdomen or genitals, in 32 per cent the extremities, and in 25 per cent the scalp, face or neck They occurred almost twice as frequently in females as in males, and were considered to be more frequent among prematurely-born infants than in NEWBORN 993

the siblings born at full term The lesions usually tended to increase in size until the patient was about six months of age and then to grow smaller until they disappeared completely, in some instances Radium was the best therapeutic agent, in the form of interstitial or external radiation, which was usually begun when the infant reached an age of three to six months, although there was no reason for delaying the treatment that long. The radium was applied at intervals of one month for four to 12 treatments. depending upon the size of the lesion The response of the angioma was usually slow at first and complete disappearance required several months of time Slow regression of the lesion was the desired result so that any reaction in the normal tissues would be avoided

The instability of the body temperatures of premature infants has been ascribed to disproportions between the production and loss of heat Respiratory metabolism of 22 premature infants has been investigated recently by H Gordon and S Z Levine 229 An average of 58 calories per kilogram of body weight was comparable to that of full term infants of approximately the same postnatal age and the same increases in metabolic rates during the first three weeks of life were observed in both groups The total number of calories produced in 24 hours by the premature infants and these figures in relation to body surface were lower than in full term infants It was questionable whether the lower rates in terms of calories per square meter of body surface of the prematures indicated a real lowering of metabolic rate or was merely an expression of the anatomic disproportion of these smaller infants between calories produced and surface area

It was also found that prematures did not lose an excessive amount of heat

by vaporization of water through the skin. H H Gordon and M D Kelley²³⁰ recorded the heat loss by skin vaporization under standard conditions in ten premature infants and found that an average of 29 per cent of the total heat production was dissipated in this manner, a figure which was only slightly greater than the average for normal infants, children and adults The higher water content of premature infants and their tendency to be more hydrolabile and to develop edema more frequently than normal infants had no effect, therefore, in increasing the quantity or rate of heat loss through the skin surface.

Normal Constituents of the Blood -The determination of the lipid content of the blood plasma of newly born infants made by E M Boyd²³¹ has indicated that the values were generally lower than those found in adults The total content of lipid found in one newborn frequently varied considerably from that of another and the quantitative relationship of the different lipids in the plasma of an infant fluctuated over wider limits than one customarily found in an adult The table of values obtained by the author with a comparison with adult values is given below The lipid content of red blood cells was found to be about the same in adults and in newly born infants

The quantities of prothrombin in the blood of newly born infants varies considerably from that in normal adults K M Brinkhous, H P Smith and E D Warner²³² stated that the amounts of prothrombin in the blood of pregnant women was very similar to that of non-pregnant women but the values in the blood of the newborn were often 14 to 39 per cent below the adult levels. The quantity gradually rose in these infants to reach average adult levels by the end of a year. One infant with a hemorrhagic

| TABLE 1 | | | | | | |
|---------|-------------|----|----------|--------|--|--|
| Lipid | Composition | OF | Oxalated | Plasma | | |

| | Adults | New-Born Infants | Values in New-Born Infants in Percentage of Values in Adults | |
|--|--|---|--|--|
| Total lipids Neutral fat Total fatty acids Total cholesterol Ester cholesterol Free cholesterol Phospholipid | 589 ± 87 154 ± 42 353 ± 56 162 ± 32 115 ± 27 47 ± 7 196 ± 23 | $ \begin{array}{c} 198 \pm 80 \\ 90 \pm 50 \\ 140 \pm 57 \\ 34 \pm 15 \\ 20 \pm 12 \\ 14 \pm 7 \\ 61 \pm 32 \end{array} $ | 34 58 40 21 17 30 31 | |

(Courtesy, American Journal of Diseases of Children, December, 1936)

tendency was found to have only five per cent of the amount of prothrombin usually found in adults. The deficiency was rapidly made up by transfusion so that normal requirements were reached at the end of ten days

The prolonged coagulation time of the blood in the newborn seems to be a natural mechanism which affords the infant protection during the first few weeks of life Histologic examination of the clotting process in abandoned blood vessels of the newborn has been made by W. A. Mulherm and J. Krafka, Jr 233 Portions of the umbilical vein, between two ligatures, were studied in serial sections at various intervals after the birth of the infant. At no time did the blood within the abandoned umbilical vessels form a true clot with fibrin formation, but it tended to deposit a hyalin material which was adherent to the endothehum of the vein Even after the cord had sloughed off from the newly born infant there was no evidence of true clot formation A true clot has never been observed in the ductus arteriosus when that vessel becomes inactive and the lumen closes Hemorrhagic lesions in the brain almost never organize to form a true fibrin clot In the presence of infection, it is possible for clotting to occur and emboli or thrombi may result. Efforts to explain the prolonged coagulation time have failed It has been suggested that the increase of bilirubin in the blood might account for the prolonged coagulation time as well as for an increase in the antithrombin content and the defective platelet formation or dissolution The authors have concluded that delayed coagulation is a protective mechanism for the newborn during the time when fetal vascular channels are being abandoned and traumatic injuries to blood vessels may occur In order to protect the infant against thrombi or emboli and similar disasters, the newly born child should be protected carefully from infections of the umbilicus, skin and mouth which might lead to the invasion of the blood stream by bacteria and thus cause the formation of true fibrin thrombi and emboli

In making comparisons of the red cell counts and hemoglobin levels of premature infants with those of full term infants, A Stewart²³⁴ observed that the initial drop in hemoglobin immediately after birth was much greater in premature infants and twins and a rise towards normal levels was much slower and never as great as in normal full term infants. The drop in hemoglobin reached its maximum in 9 to 12 weeks and the color index tended to remain at figures of one or more throughout the same period of time. This is in contrast

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to the course of events in older children where the number of red cells tended to remain the same but the hemoglobin content fell to as low as 15 per cent.

Hemorrhage of the newborn occurred in a group of 61 patients observed and reported by N. B Capon 235 He eliminated from his series those infants who tended to bleed from secondary causes such as trauma, slipping of cord ligatures, syphilitic infections, and those who had blood in the stools because of an enteritis or because blood was ingested from the birth canal or from the mothers' breasts The location of the bleeding in most of the 61 patients was the gastroenteric tract, with melena in all cases and hematemesis in a fairly large percentage, but the nose, pharynx, umbilicus and vagina were involved in single instances Hemorrhage occurred in only one case in every 405 live births. The average time of the onset of bleeding was 41 hours after birth and the occurrence of the symptom seemed to be unrelated to the age of the mother, the type of delivery, the birth position of the infant in the family or the weight of the baby Treatment of the hemorrhage included such general measures as the maintenance of body heat and the building up of the infant's nutrition with proper diet, but most important was the intramuscular injection of whole blood Intravenous transfusions were necessary when the hemorrhage was severe or did not respond to the other procedures

Icterus Gravis Neonatorum

The subject of icterus gravis neonatorum has been reviewed by M. Astrachan ²³⁶ The six patients whom he reported had the typical symptoms of the early appearance of severe jaundice, enlargement of the liver and spleen, increased numbers of nucleated red cells and immature forms of leukocytes in the

blood, the presence of bile in the urine, a positive direct van den Bergh reaction, and at post mortem examination, the finding of hematopoietic foci in the liver Without treatment such patients die rapidly but the administration of whole blood intramuscularly, or better, by transfusion into the veins, may lead to recovery A family history of jaundice in other members of the family is usually obtained and in such instances the early administration of whole blood to the newly born infant may prevent the development of severe symptoms The author had one such patient in which this procedure probably had considerable prophylactic value Hemolysis of the red cells seems to be of secondary etiologic importance and the author supported the theory that there is a deficiency of an antihemolytic factor in such patients In utero the infant receives sufficient amounts of this material from maternal sources, but loses it rapidly after birth so that it must be replaced by transfused blood

Many studies of the etiology of this condition are in progress M M Wintrobe, R E Kinsey, R C Blount and W Trager^{2,37} found that the administration of liver extract to pregnant rabbits of its injection into their placentas, had no effect on the blood of the fetuses Fetal livers and placentas had no antianemic substances but did contain growth factors necessary for mosquito larvae. The experiments suggested that anti-anemic substances might play a rôle in the fetal hematopoiesis but was not definite proof.

From a statistical analysis of the reports in the medical literature of icterus gravis neonatorum, hydrops foetalis and congenital anemia, M T Macklin²³⁸ found that these diseases have hereditary characteristics suggesting dominant mu-

tations. This is especially illustrated by icterus which seems to occur in about 50 per cent of the offspring of a family Hydrops foetalis occurs in families in which miscarriages and still-births are frequent. If these deaths are due to this disease, the author concluded that it also was due to a dominant mutation. Congenital anemia does not occur in half of the children of a family and is limited to races of the Mediterranean Sea but taking all cases into consideration, the possibility of a dominant mutation is again strong Each of these diseases occurs more frequently alone than in combinations, in individual families, a factor which argues for dominant mutation as the etiologic factor, but varieties and combinations are possible The increasing frequency of such illnesses may be due to better diagnostic methods but the author believed that the saving of infants with these disturbances is much more common since the value of blood transfusion has been recognized, and such patients consequently live to a reproductive age and multiply the chances of transmission of the characteristics to their children

Blood serum, instead of whole blood, for the treatment of anemia associated with jaundice in the newborn has been recommended by G N Krost 239 In three newly born infants with severe jaundice and in one with an erythroblastic type of anemia, 10 to 15 cc of the maternal blood serum were administered with good results. The substances necessary to check hemolysis of red cells and to stimulate their normal production in the infant seem to be present in the serum rather than the cells of the maternal blood The cellular elements in the transfused blood which contain pigment which might aggravate the jaundice, need not be administered to the infant

Intestinal Obstruction

The symptom of persistent vomiting in the newborn should always suggest the possibility of obstruction of the alimentary tract. In the eight cases reported by H. A Reisman, 240 this was a common symptom and was accompanied frequently by distention, constipation or mucous stools, and loss of weight The majority of patients with obstruction of the intestinal tract owe that condition to congenital lesions but occasionally intussusception or peritonitis may be the The most frequent site for obstruction is the ileum followed in order by that of the duodenum, colon and the esophagus Obstruction of the esophagus frequently occurs at the level of the bifurcation of the trachea and in such cases the esophagus may communicate with the trachea producing symptoms of cyanosis, coughing and râles in the chest Partial atresia may occur in any portion of the intestinal tract but it is more common to find that the obstruction is complete with the gut terminating in a blind pouch The use of barium is often of great assistance in making a diagnosis and early surgical treatment is highly essential as the only curative method. It was interesting to note that in the series of patients reported by the authors, seven of the eight infants were of the male sex

Intestinal obstruction due to meconium ileus is a less common type. In the report of an infant by K. Dodd,²⁴¹ the meconium was found to form a mass in the ileum which was accompanied by pathologic lesions of the pancreas. Twenty-one cases of a similar nature were found to have been reported in the literature previously. The symptoms of this type of obstruction are very similar to those produced by other types of obstructive lesions but distinctive features in the majority of instances are the

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putty-like consistency of the meconium, probably due to disturbances of the secretion of the pancreas or liver

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In the report of two cases of complete duodenal atresia, J Rose and A M May, Jr, 242 call attention to the fact that the most prominent symptom is the vomiting which commences at the time of birth and thus makes a little earlier appearance than in the case of patients with pyloric stenosis The diagnosis can often be made by roentgenologic examination of the intestinal tract and by the absence of keratinized cells and lanugo hairs in the examination of the stools The authors warn against the use of gavage in feeding infants with such symptoms until the possibility of obstruction of the intestinal tract is eliminated. The treatment is entirely surgical and in order to be successful it must be practiced early in the infant's life

Traumatic Injuries

Brain injuries of the newborn can be diagnosed in some instances by the use of encephalography. J. L. Law²⁴³ has employed this method in the examination of 17 infants who had some defect of the central nervous system resulting from cerebral injury before birth or from developmental defects. Ten of this group had coentgenologic evidence of cerebral atrophy, two had arachnoid adhesions, five had a similar condition associated with other lesions, one had a porencephalic cyst, two had porencephaly with other lesions, and two had dilatation of the ventricles or of the basal cistern

Among 27 infants with such conditions as mental retardation, hemiplegia or Little's disease, who were thought to have received intracranial injury during birth, encephalography demonstrated dilatation of the ventricles in seven instances, together with certain other pathologic conditions. The authors considered enceph-

alography to be a safe procedure and they were able to obtain complete filling of the ventricles with air in about 70 per cent of a series of 121 trials. In only about five per cent of the operations was it impossible to displace the fluid with air and in 25 per cent the filling of the ventricles was incomplete.

Small Intracranial Hemorrhages-These occur frequently in the newborn and even gross hemorrhage may not produce severe symptoms for several days This statement, made by R H. Nattrass.244 was followed by a review of the chief clinical signs of intracranial hemorrhage Most frequently observed were asphyxia, usually of the pallid type, attacks of cvanosis, a slow or irregular respiratory rhythm, and less frequently, neck rigidity, unequal pupils, nystagmus or strabismus and an impairment of the sucking reflex Lumbar puncture was thought to be an essential procedure for both the diagnosis and the treatment of intracranial hemorrhage Other methods of treatment were symptomatic, and included resuscitation efforts at birth, tube feeding when the sucking reflex was abolished, oxygen and carbon dioxide inhalation for cyanosis, quiet rest in a darkened room without attempting breast feeding until the condition of the infant improves

Paralysis of the Radial Nerve—In the newborn this has been observed recently by S M Abelson and J Greengard ²⁴⁵ Symptoms of this condition included a flaccid paralysis of the extensors of the wrist with a resulting wrist drop and slight adduction of the thumb. The hand and forearm were placed in a splint and the muscles were massaged daily for a period of two weeks, by which time recovery was complete. The condition seemed to be the result of pressure on the upper arm during delivery, although possibly the intoxication from

barbiturates or quinine administered to the mother during the time of delivery was a contributing factor

Infections

The time at which micro-organisms enter the intestinal tracts of the newborn has been investigated by M L Snyder 246 Bacteria in the meconium of newly born infants were found in three instances of a series of 29 specimens collected within 30 minutes after delivery Types of acidophilus, streptococcus and colon bacıllı were the microorganisms found In specimens collected from ten infants 30 to 60 minutes after delivery, plate methods of culture showed no organisms but with an enriched medium, bacteria were obtained in four instances In a group of 16 infants, the stools collected one to two hours after delivery contained no organisms by plate culture, but bacteria were recovered in all but six cases by the use of enriched media Stools passed two to three hours after delivery were sterile by plate culture except in one patient, but by the use of enrichment methods bacteria could be demonstrated in all but two patients Cultures were made of the bacteria obtained from the skin area about the anal region. In four patients no bacteria could be obtained by this method, in four other patients the types of micro-organisms differed from those found in the meconum and in four instances the types of bacteria were found to be the same in both the skin and in the meconium. The authors felt reasonably sure that the bacteria found in the intestinal tract of newly born infants had gained entrance through the mouth from the swallowing of amniotic fluid infected by the bacterial flora of the vagina

In a few instances bacteria can be recovered from the intestinal contents of stillborn infants M L Snyder²⁴⁷ was

able to isolate organisms from the intestinal contents of the ascending colon of two patients of a group of 15 still-born infants. In one instance, the bacillus welchn could be found microscopically and by culture methods in the duodenum, the ileum, the ascending and descending portions of the colon In four instances bacteria could be obtained by plating methods from the intestinal content of various locations in still-born infants The possibility of contamination of media used in certain methods made it questionable whether bacteria were present in the intestinal tracts of all of these infants It has been suggested that septicemia might be one of the causes of bacteria invading the intestinal tract before birth but in one such case noted by the authors, the organisms isolated from the blood stream were not the same type as those found in the intestinal contents Infection by way of the amniotic fluid, especially when the fetal membranes ruptured early, may have allowed bacteria from the vagina to enter the mouth or rectum of the fetus in four instances of the author's series of patients since the micro-organisms found in the two localities were the same types. However, the size of the series was not large and there remained some question in regard to this method of infection of the infant. The possibility of the infant's intestinal tract becoming infected during the passage of the fetus through the birth canal was likewise considered, but could not be proved in this group of experiments

Infections of the Umbilicus—Occurring in a large group of newly born infants these have been surveyed recently by J W Chamberlain ²⁴⁸ In the group of 74 patients who were admitted to the hospital with such infections over a period of ten years, the condition was present as an incidental infection in 23 instances and was the primary cause for

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admission to the hospital in the remaining 51 patients Among these children who, of course, represented the group with the most severe types of infection of the umbilicus, the mortality rate was 65 per cent and the causative organisms were most frequently the streptococcus hemolyticus and staphylococcus aureus. The ages of the majority of the infants were one to three weeks The common manifestation of the umbilical infections was a purulent discharge or crusting of the umbilicus surrounded by an area of Peritonitis ocredness and swelling curred in 15 instances, abscesses of the soft tissue in 15 and cellulitis or erysipelas in 12 Other lesions, such as osteomyelitis and meningitis, were observed, but hemorrhagic lesions were noted in only three instances The prognosis in such cases seemed to depend entirely upon the extent of the lesions and the presence of severe complications

Meningitis of the Newborn-This is a rare condition and many of the common symptoms and clinical signs of the disease in older patients are absent in this age group. Of the 21 newly born infants with meningitis observed by W S Craig,249 the majority had been boin prematurely Common symptoms of the disease in this series of infants were restlessness, a loss of appetite and decreases in weight and strength Often there was pneumonia or infection elsewhere in the body which gave more striking and localizing symptoms Common findings suggesting the intracranial infection were certain ocular signs, such as inequality of the pupils, muscular incoordination and in a few instances, a bilateral nystagmus Tendon reflexes were usually unchanged from normal although they seemed to be exaggerated in a few patients

Such signs as the positive Babinski reaction and rigidity of the neck were not

universally observed and convulsions occurred in only a few patients, just before their death. A bulging and spongy resistance of the fontanels which was a fairly common manifestation of meningitis was often interpreted as evidence of an intracranial hemorrhage Fever did not develop in all patients and in some cases the temperature was subnormal until a few days before death when a steady rise occurred A possible cause for the meningitis was septicemia which frequently was noted in these infants but it was impossible to decide in most instances whether the organisms reached the meninges by way of the blood stream or by direct extension from infections of the nose and mouth

Infections of the skin and mucous membranes occurred in 15 infants of this series and possibly these lesions led to the development of meningitis, especially when the middle ear became infected as was the case in a few instances types of organisms found in the meninges or in the spinal fluid were most frequently the bacillus coli, although others, some of them of an unusual nature, were also isolated. The diagnosis was confirmed in every instance by abnormal changes in the cerebrospinal fluid Clinical signs suggesting an intracranial disturbance, the ocular manifestations, together with expressions of fear and a restless movement of the head which developed after the first week of life, were thought to suggest meningitis Intracranial hemorrhage, especially when located in the ventricles was more apt to begin abruptly with more severe symptoms, the fontanel was more bulging and tense, the cry more shrill and the convulsive movements were of a gross nature The high temperatures accompanying intracranial hemorrhage were limited to the terminal stages rather than lasting for two to four days as in meningitis

Prevention of meningitis in the newborn should be directed towards the prevention of infections of all sorts, with special attention to the hygiene of the skin, mouth, eyes, nasal and ear passages.

Gastroenteritis of the Newborn-The characteristics of severe gastroenteritis in newly born infants have been reported by W. S Craig 250 During a period of 3½ years, 41 cases were observed in the Royal Maternity Hospital in Edinburgh Of this number, 11 died. The symptoms consisted usually of loss of appetite, listlessness, loss of weight and an increased number of stools which became watery in consistency, and green or brown in color A degree or two of fever and dehydration were noted frequently The gastroenteritis seemed to occur in epidemics and the author thought the disease resulted from the ingestion of some food elements or bacteria associated with the artificial feeding, since the infection rarely occurred in breast-fed infants Treatment consisted of the removal of milk from the diet and the administration of weak tea or glucose solutions Saline solution containing five per cent dextrose was given subcutaneously in amounts of 1 to 1^2 , oz (30 to 50 cc) daily Gastric lavage and washing of the lower bowel with liquid petroleum lett in the rectum were therapeutic measures resorted to in some patients. The prevention of infection elsewhere in the body was an important factor in guarding against the occurrence of gastroenteritis and the development of complications

Previous reports in the medical literature have stated that antibodies of diphtheria, scarlet fever, poliomyelitis and typhoid pass through the placenta from the mother to her newly born infant Agglutinins of B coli, however, did not seem to be transferred in this manner

To test this problem further J Felsen and A. G Osofsky²⁵¹ examined the agglutination titers of 100 mothers and their babies, against six strains of dysentery bacıllı. In most instances, the infants had the same type of agglutinins as their mothers but in smaller amounts In no instance did agglutination occur with the serum of the newborn in dilutions of one to 160 or more thors believed that the failure of transmission of protective bodies against the dysentery bacilli to the newborn accounted for the severity of that illness during the first few days of life protect young infants from such infections, they advised the careful search, both bacteriologically and clinically for evidence of such infections, and special precautions against contamination from food, from nurses and other employees engaged in the care of the newborn

Tetany

Common symptoms of tetany in seven newly born infants observed by C E Snelling and A Brown²⁵² consisted of twitching, evanosis and convulsions The diagnosis in these cases was made by the examination of the blood calcium which in every instance was less than eight milligrams per 100 cc of blood serum. In one instance the calcium was as low as 39 milligrams per cent Treatment consisted chiefly of the injection of solutions of calcium gluconate intramuscularly or intravenously and the administration of calcium chloride and viosterol by mouth The incidence of tetany has changed in its age distribution in recent years so that now it is seen more frequently in the early weeks of life rather than the later months of the first year It still occurs more often in the winter months from January to March than in any other season

NEWBORN 1001

The treatment of tetany with a double calcium salt produced considerable improvement in the group of ten newly born infants observed by H R. Litchfield 253 Clinical symptoms of the condition, consisted of irritability, crying, tonic or clonic twitching of the muscles following stimuli of sound or touch, a positive Chvostek reaction and hypertonia The blood calcium values ranged from 79 to 82 in most instances The medication containing calcium lactobionate and calcium bromide raised the blood calcium to higher levels than developed spontaneously in a control group This form of therapy also of infants tended to reduce the hyperactivity of the patients

Pneumothorax

Pneumothorax of the newborn is a relatively rare condition. In the case reported by S J Wilkinson²⁵⁴ the pneumothorax was apparently due to an infection which led to septic emboli in the lungs, one of them near the pleura so that it caused the collapse of the lung Only two other similar on that side instances have been reported and each followed an infection elsewhere in the body, possibly an omphalitis or an infected circumcision wound. In the baby observed by the author a staphylococcus was the type of micro-organism recovered and the infection was widespread, producing an empyema, fistulae between a small bronchus and the pleural cavity, pericaiditis, endocarditis of the aortic valve and involvement of the liver, kidneys and myocardium with degenerative changes The author was able to find 17 previously recorded instances of pneumothorax in the newborn, due sometimes to congenital defects of the lung development or to mechanical factors resulting from trauma, cough or enlargement of the thymus Previous reports by other authors indicated that primary infections of newborn frequently involve the lungs and the occurrence of septicemia following infections of the umbilical stump or circumcision wounds should be suspected in all instances. Treatment of infectious pneumothorax gives little hope and the important factor is its prevention by the early observation and treatment of the primary foci of infection.

An instance of pneumothorax in the newborn apparently produced by traumatic puncture was reported by J S Leopold and F. Castrovinci ²⁵⁵ In attempts to resuscitate the infant, medication was supposedly injected into the heart but the authors believed that the pleural cavity was entered which allowed the lung to collapse Within seven days the air in the pleural cavity had been absorbed and the lung expanded to its normal position

Lesions of the Bones and Muscles

A condition of the newborn described as lacunar skull was reviewed recently by H B Rothbart, 256 and eight such cases were reported The condition is frequently associated with spina bifida, meningocele or encephalocele and can only be recognized by roentgenography or at autopsy In the roentgenogram the inner table of flat bones of the skull. especially in the frontal and parietal regions, appears uneven with variations of thickness The lacunae are the rarefied portions and do not seem to conform to the outline of the brain tissue The lesions do not increase in size after birth The etiologic factors have been ascribed to (1) an increase in intrauterine pressure, (2) a nutritional disturbance leading to an ischemia which disturbs normal ossification, or (3) dis-A histologic study of the skull bones in two patients led the authors

to believe that the defects were the result of a primary deficiency in the ossification process.

Bismuth employed in the treatment of syphilis of pregnant women may be deposited in the long bones of their infants This condition has been observed by J. Caffey.²⁵⁷ The lesions correspond to those produced by lead poisoning and appear in roentgenograms as transverse lines of increased density near the ends of the shafts of long bones The author was able to demonstrate such lines in newly born nonsyphilitic infants whose mothers had received as little as a single course of treatment with bismuth early or late in pregnancy Similar lesions were produced experimentally in growing dogs by the administration of bismuth Although the roentgenologic appearance of lead and bismuth deposition is the same, certain histiologic differences can be ascertained Bismuth deposition seemed to be more dependent upon the calcium content of the cartilaginous matrix than upon the total amount of bismuth present, a condition not analogous to that of lead deposition

Congenital Muscular Hypertrophy - This is a rare condition in newly born infants and was reported by B E Hall, F W Sunderman and J C Gittings 258. The patient was a colored infant with a symmetrical increase in the size and strength of his muscles, an associated mental retardation, and evidence of extrapyramidal motor disturbances consisting of hypertonicity, resistance to passive motion, slight rigidity of the neck and a tendency to assume a position of opisthotonos Blood chemical studies showed high concentrations of potassium and inorganic phosphorus and phosphatase An examination of the urine indicated the excretion of large amounts of creatine and creatinine which the authors believed might be due to an increased muscular development and higher rate of metabolism. Only four other such cases had been reported previously in the medical literature and three of these patients had some similar symptoms although not all of the characteristics of the child reported above

The ease with which young infants lose weight and tissue fluids has suggested a very labile water holding mechanism. The analysis of muscle tissue of the newborn has been reported by E Kerpel-Fronius 259 The figures show higher chloride, sodium and water contents of muscles of young infants, and relatively low protein, nitrogen and potassium values These conditions simulated edema in older patients where the water is held in a labile form in the interstitial tissue Newly born infants lose this water rapidly under certain conditions of disease or nutritional disturbance

Internal Glandular Disturbances

Marked decreases in the size of the adrenal glands of infants during the first few weeks of life were not accompanied by any biochemical changes of the blood as far as could be determined by H Bruch and D J McCune 260 It seems that the large relative size of the inner zone of the adrenal gland begins about the fourth month of fetal life, reaches a maximum at the time of birth and decreases rapidly during the first six weeks of life Deprivation of this cortical substance, as determined from animal experiments and observations of patients with Addison's disease, results in increases of the quantity of sodium in the blood and the total amount of water excreted by the kidneys Tests made by the authors of the sodium content and specific gravity of the plasma, the cell volume and nonprotein nitrogen of 106 specimens of cord blood from 72 infants during the first three weeks of life gave values identical with those of healthy children and adults and, therefore, did not indicate any dysfunction of the adrenal glands in the newborn

Infants Born of Diabetic Mothers

The care and treatment of infants born of diabetic mothers has been given especial consideration by L M Randall and E H. Rynearson 261 Inadequate production of insulin by the mother is usually compensated by an increase of pancreatic activity of the fetus fetus tends to be larger than average and miscarriage or death before birth has frequently occurred When the infant is born alive, its pancreas tends to produce more than adequate supplies of insulin and a condition of hypoglycemia results, with symptoms of evanosis and muscular twitchings or convulsions The authors recommend careful observation and treatment of diabetic mothers during pregnancy, delivery of the babies of diabetic mothers a few weeks before term by caesarean section, and careful observations of the blood sugar levels of the mother, the cord and of the infants during the first few days of life until normal sugar metabolism is established Of a group of seven pregnant mothers, six were delivered by caesarean section in the 33rd to 37th week of pregnancy. Blood sugars of three infants were at levels slightly above 40 mg per cent at the time of birth and the others showed symptoms of hypoglycemia within the first three days of life Treatment of such infants consisted of intramuscular injections of ten per cent dextrose solutions, the early and frequent feeding of ten per cent dextrose or lactic acid-karo solutions, and frequent determinations of the blood sugar levels Since these infants were prematurely born, the special attention and care necessary for such immature patients was an important part of the treatment

Sclerema Neonatorum

This has seemed to be related to a disturbance in water metabolism, according to E Schulze ²⁶² He has attempted to treat the condition by administering *thyroxine* intramuscularly. This seemed to reduce the swelling of the skin and subcutaneous tissue, and to increase the urinary output. It gave better results than any previous types of therapy, such as *massage* or the *application of heat*

NUTRITION AND NUTRITIONAL DISTURBANCES

By WALDO E NELSON, AB, MD

Vitamin A

The vitamin A reserve of the human infant and child during health and disease has been estimated by J B Ellison and T. Moore ²⁶³ Determinations of the vitamin A content of the liver were made in about 200 children under 15 years of age dying by accident or from disease. It was found that the vitamin

A reserve was very low in infants under four weeks of age and that after the first four months of life the reserve rose to a much higher level. It was estimated that a diet of cow's milk, and probably also human milk, should contain sufficient amounts of vitamin A to permit the accumulation of reserves of the order of magnitude observed. Attention

was called to the possibility that if a mother, having a vitamin A reserve equal to the typical value found in health, were restricted during lactation to a diet deficient in vitamin A, her total secretion, if maintained at the normal rate, would represent almost the entire liver reserve. The vitamin A reserves noted in various diseases were as follows: high reserves in tuberculosis, moderate reserves in measles and low

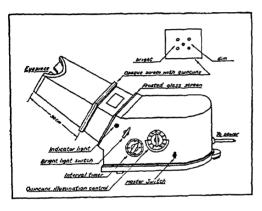


Fig. 1—Schematic representation of the biophotometer (Courtes), Jour A M A, Feb. 6, 1937.)

reserves in pneumonia, head infections, septic diseases and heart disease. A comparison of the reserves found at autopsy in nine cases of measles treated with vitamin A concentrates with those found in a series of similar, untreated cases indicated that the percentage of vitamin A ingested which is stored in the liver may at times be quite low

Studies to determine the effect of anadation on the ritamin A content of eraporated milk have been conducted by H. J. Cannon and O. F. Hixson 264. No differences were detected between the vitamin A content of irradiated and non-irradiated evaporated milk. In each milk, the vitamin A content was 1767 units per 14.5 avoirdupois ounces and the vitamin A content of 350 mg of either irradiated or non-irradiated evaporated evaporated or non-irradiated evaporated.

orated milk was equivalent to the vitamin A contained in 0.5 mg of U S P cod-liver oil. In other words, irradiation of evaporated milk has no effect upon the vitamin A content.

Studies on hypovitaminosis A by C Friderichsen and C Edmund²⁶⁵ indicate that a mixed diet containing vegetables results in a better fixation of vitamin A in the infant's tissues than does a diet of milk alone. The vitamin A content is measured by means of the authors' test of reflex irritability of the eve to light, so-called minimum reflexible. Diets with low fat content such as buttermilk and protein milk may cause a vitamın A deficiency if administered for some time. Despite the large amount of carotene in mashed carrots and carrot juice, they are not always capable of preventing latent avitaminosis A contrast, a preparation of spinach (dried spinach) showed a rapid and more stable effect notwithstanding the smallness of the dose when measured in international (USP) units of vitamın A

Additional studies by means of a new photometer for the dark adaptation test for the detection of vitamin A deficiency have been carried out by P C Jeans, E Blanchard and Z Zentmire 266 Adaptation of the normal eye depends on the ability to regenerate visual purple, which is related to the presence in the retina of vitamin A, or a closely related sub-Consequently, any test that shows relative or absolute capacity for dark adaptation becomes a test for vitamin A deficiency in persons with potentially normal eyes (Scotopic vision is measured after alternate periods of exposure to bright light and to darkness) The observations are made by determining the amount of light necessary for the subject to see holes in a metal screen when the light transmitted through the holes is of decreasing intensity from the left to the right of the quincunx (See Fig 1)

The photometer is installed in a dark room, which is kept in as nearly absolute darkness as possible throughout the test. It is theoretically possible to conduct the test in a lighted room, but this is not a practical procedure. The eye piece of the photometer is so shaped that, as the subject looks into the instrument, he can press his head against the soft rubber edge and exclude most extraneous light. Personal comfort of the

Cleveland. The examination of children by means of this photometer indicates that vitamin A deficiency is more frequent than has been generally assumed On the basis of their studies with the photometer, the authors have attempted to determine the vitamin A requirements of children. They have evidence suggesting that 3000 units daily will satisfy the requirement of 10- to 11-vear-old children.

Among others, C. E Snelling²⁶⁷ has been unable to verify the results of Jeans and Zentmire and is inclined to doubt

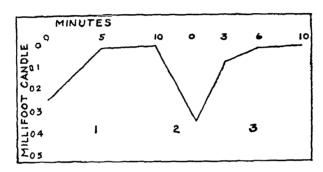


Fig 2—Plotted readings of a test of a normal subject 1, Foreperiod, 2, light period, 3, recovery period (Courtesy, Jour Amer Med Assoc, Feb 6, 1937)

subject is considered important Between readings, opportunity should be offered for relaxation against a back support. The time consumed by the test comprises a total of 23 minutes divided into three periods. (1) A ten-minute preliminary period in the dark, (2) exposure to the bright light of the photometer for three minutes, and (3) a ten-minute period in the dark.

Readings are made in the beginning, middle and end of the preliminary period and at the beginning and end of the recovery period, with one or two additional readings in the recovery period between the first and last readings. More complete details may be had from the original article, or from the manufacturer, Frober-Faybor Company of

that the photometric test is satisfactory for the estimation of small variations in dark adaptation, such as might be produced by vitamin A deficiency

Vitamins A and B

Determinations of the vitamin A and B content of canned strained vegetables have been made by F Hanning ²⁶⁸ The range of vitamin A content of canned strained spinach for a period of two years was from 3339 to 3594 international units per ounce, for carrots, 1792 to 1887 units, for tomatoes, 1108 to 1326 units, for peas, 270 to 327 units, and for green beans, 196 to 344 units. The vitamin B content of canned strained tomatoes was from 70 to 121 international units per ounce, of peas,

82 units; of carrots, 30 units; of green beans, 30 units; of beets, 10 units, and of spinach 16 units. The vitamin A determinations conformed fairly well with those made in the preceding two-year period except for an improvement in peas and green beans.

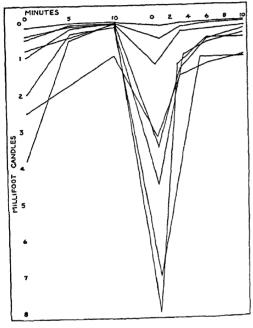


Fig 3—Plotted readings indicating the range of values found when a large group is tested (Courtesy, Jour A M A, Feb o, 1937)

The vitamin B determinations varied somewhat from those previously reported by the author. This was especially true for peas which were twice as potent in 1934 as in 1932.

Vitamin C

Ascorbic Acid Oxidase — It has been shown by H Tauber²⁶⁹ that certain plants such as Hubbard squash and summer squash contain a powerful enzyme which rapidly oxidizes vitamin C, although these plants contain none of this vitamin In view of these observations, this author decided to find out whether the vitamin C content of juices

of citrous fruits, which are excellent sources of vitamin C, are exposed to the destructive action of this ascorbic acid oxidase. His results indicate that there is no ascorbic oxidase in these fruit juices and that the vitamin keeps fairly well for at least five hours at 100 4° F (38° C.). Similarly no ascorbic acid oxidase could be demonstrated in cow's milk. The slight destruction of vitamin C which was observed in cow's milk was thought to be due to traces of copper in the milk introduced by feedings or by technical means.

The clinical methods for the determination of reduced ascorbic acid content of blood plasma described by Farmer and Abt have been confirmed by L D Greenberg, J F Rinehart and N M Phatak ²⁷⁰ However, it has been shown by M Pijoan, S R Townsend and A Wilson²⁷¹ that the ascorbic acid value of blood is materially affected by standing, either in the icebox of at room temperature. Determinations should be carried out within one-half hour after the collection of the blood

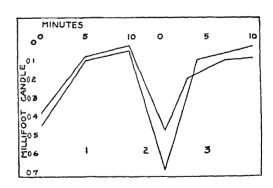


Fig 4—Two types of borderline curve (Courtesy, Jour A M A, Feb 6, 1937)

The rate of urmary excretion of test doses of ascorbic acid in saturated and unsaturated subjects has been determined by E E Hawley and D J Stephens.²⁷² In regard to the total excretion of ascorbic acid in unsaturated

subjects their results were in agreement with others who have shown that the administration of a large test dose of ascorbic acid to a subject whose stores of vitamin C have been depleted results in the excretion of an amount of ascorbic acid but little, if any, larger than that excreted during a control period without the test dose. In addition the rate of excretion of ascorbic acid in saturated and unsaturated subjects over a 24-hour period was also shown to be

G. J. Everson and A. L. Daniels.²⁷³ It was shown that urmary excretion of ascorbic acid tended to parallel the intake, notwithstanding the fact that retention at certain levels of ingestion was considerably below the physiologic optimum. Retentions of ascorbic acid paralleled the ingestion only up to 75 mg or thereabouts per kilogram. Higher ingestions were without influence on the retentions of the children studied. The highest retentions were obtained with

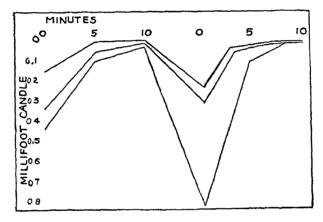


Fig. 5—Test results showing improvement obtained in ten and sixteen days respectively with 20,000 units of carotene daily (Courtesy, Jour A. M. A., Feb. 6, 1937)

different In those subjects whose reserves of vitamin C have been depleted, there was only a slight increase in the rate of excretion during the first few hours regardless of whether the ascorbic acid was administered by mouth or intravenously In subjects saturated with ascorbic acid, an average of 80 to 85 per cent of the total 24-hour excretion occurred during the first 12 hours after administration of the test dose the latter was given intravenously maximum excretion occurred during the first and second hours After oral administration, maximum excretion occurred during the third, fourth, fifth and six hours

Vitamin C studies in children of pre-school age have been carried out by

the youngest child, suggesting that there is a greater demand by younger tissue for vitamin C. Comparable amounts of commercial ascorbic acid and ascorbic acid from foods resulted in similar retentions.

It has been shown by F T Chu and C Sung²⁷⁴ that, while there is a fluctuation in the vitamin C content of lactating mothers corresponding to the increase or decrease of the vitamin C intake in the diet, these changes are slow and steady, being entirely different from the rapid response in the urinary excretion. It is felt that, since milk is a product of secretion rather than excretion, it behaves like the body tissues in this respect

The effect of the administration of sodium bicarbonate and ammonium chloride, in amounts sufficient to induce marked changes in the hydrogen ion concentration of the urine, on the excretion of ascorbic acid has been studied under controlled conditions of vitamin C depletion and saturation by E E Hawley, J P Frazer, L L Button and D. J. Stephens 275 The ascorbic acid content of the urine was consistently and significantly lowered during periods of sodium bicarbonate administration, when the urine was highly alkaline, as compared with similar periods of ammonium chloride administration with a highly acid urine The practical implications of these observations are not clear but they would appear to indicate that in evaluating the results obtained by studying the vitamin C content of the urine in any subject, one should know not only the dietary history of that person but the approximate HH of the urine at the time of study

Observations on the relation of vitamin C metabolism to rheumatic infection in children are reported by M A Abbasy, N. G. Hill and L. J. Harris 276 They observed that distinctly less vitamin C was excreted in the urine of children with active or convalescent rheumatic fever than in the urine of control children. The authors are not willing to participate in the argument whether the vitamin C deficiency is a cause or an effect of the rheumatic infection. They do interpret their observations, however, as indicating the need for the administration of large amounts of vitamin C both therapeutically and prophylactically They do not state whether the children were receiving salicylates during the test periods

Data are presented by A L Daniels and G J. Everson²⁷⁷ which appear to indicate that acetylsalicylic acid

(aspurn) increases the urinary excretion of vitamin C. They suggest that further studies of conditions affecting ascorbic acid elimination may explain the frequently observed association of scurvy and rheumatoid arthritis, when sodium salicylate has been administered therapeutically.

In contrast to the observations of Daniels and Everson, J B Youmans, M B Corlette, H. Frank and M Corlette²⁷⁸ did not observe any significant effect of acetylsalicylic acid ingestion upon the excretion of ascorbic acid in the urine The observations by these authors were made on adults, and on children as in the study by Daniels and Everson Acetylsalicylic acid was administered in amounts as great as 40 grains (2 6 Gm) per day.

Scurvy

The excretion of ascorbic acid in the urine and its concentration in the blood plasma have been studied in seven cases of infantile scurvy by T H. Ingalls 279 Absolute depletion of ascorbic acid in the urine and very low values in the plasma were found Vitamin replenishment was accomplished quickly or over a long period of time, depending primarily on the dose of ascorbic acid employed The author believes that greater emphasis should be given the quantitative aspects of ascorbic acid therapy since approximately 1000 mg or the equivalent of 2 liters of orange juice were required to affect perceptibly the absolute urmary depletion of the infants in this series of cases Each infant required about 2000 mg before even partial saturation was obtained In addition to the studies of ascorbic acid content of the plasma in infants with scurvy, ascorbic acid determinations of the plasma were also performed in a group of well babies and a group of babies picked at random from the hospital ward These observations

TABLE I.

| State of Vitamin C Nutrition | Plasma Ascorbic Acid (Mg Per Cent) | |
|---|---|--|
| Optimum Saturation Normal Low normal Suboptimum Asymptomatic Deficiency Scurvy Scurvy | 2 00-1 00 1.00-0 70 0 70-0 50 0 50-0 30 0 30-0 15 0 15-0 | |
| | | |

showed ascorbic acid levels of the plasma which were generally characteristic of optimal and suboptimal intake of vitamin C. This material indicates a probable correlation of plasma values for ascorbic acid with the nutritional state of the patient. The arrangement is shown in Table 1. It is suggested that perfection of the method for determination of plasma ascorbic acid may ultimately result in a test by which it will be possible to detect the existence of scurvy before the appearance of the characteristic signs or ioentgenologic changes

Titamin D A biologic test to determine the vitamin D content of human serum by its curative effect on rachitic rats has been devised by J Warkany 280 Measured quantities of human serum are fed to rachitic rats and the amount necessary to produce healing of the rickets is determined. The results are expressed in number of rat or U S P units per 100 cc of blood serum.

It is stated that this method is not necessary in the diagnosis of infantile rickets when adequate information can be obtained from clinical and roentgenologic data and from a determination of the phosphorus content of the blood. It may be of value, however, in those instances in which clinical and roentgenographic findings do not agree with the chemical studies and in those rare instances in which rickets resists vitamin D treatment. This method of direct esti-

mation may also be applied to studies of the etiology of diseases of the bone to be distinguished from rickets, such as celiac rickets, renal rickets or the various forms of osteoporosis.

On the basis of their accumulated data, N Morris, M M. Stevenson, O. D. Peden and J M D Small²⁸¹ believe that the elevation of the plasma phosphatase is an earlier manifestation of rickets than may be determined by either clinical or radiologic examination noted a rough parallelism between the height of the phosphatase and the severity of the rachitic process, but they point out that the level of the phosphatase cannot be taken as an index of the severity in the individual patient. A moderate degree of correlation was noted between the rise in phosphatase and the fall in phosphorus and in the calcium-phosphorus product, especially with the latter. However, it appeared that of the three, an increase in plasma phosphatase was the most delicate test of active rickets It is pointed out, however, that an alteration in phosphatase alone is not conclusive evidence of the presence or absence of rickets. In untreated active rickets the plasma phosphatase continues to rise Administration of vitamin D prevents this rise and in two to three weeks causes a drop in the phosphatase level The rate of decline depends upon the dosage of vitamin D and is much more rapid with large amounts With ordinary therapeutic doses normal phosphatase levels may not be reached for over three months

Likewise, the observations of D J Barnes and M. D Carpenter²⁸² indicate that serum phosphatase is a more accurate indicator or measure of rachitic activity than is the serum phosphorus determination. Their data also indicate that normal serum phosphatase range for infants is between 6 and 125 mg per cc

Antirachitic Agents

A study of the comparative value of cod-liver oil. viosterol and vitamin D milks in the prevention of rickets has been conducted by M M. Eliot and M. Nelson, D J Barnes, F A. Browne and R M Jenss 283 They point out the necessity of considering such factors as color, sex, rate of growth in length, period of observation, and interval between examinations, in the evaluation of certain types of antirachitic substances when they are administered at different dosage levels for the prevention of rickets. When pertinent basic factors were taken into consideration, it was apparent, that, in spite of their lower dosage level, the milks, especially those at the 400 unit level, tended to be more effective in the prevention of rickets than cod-liver oil There was also evidence that viosterol was at least as effective as cod-liver oil, and no evidence that cod-liver oil was superior to viosterol, unit for unit, in the prevention of rickets There was no definite evidence that one type of milk at the 400 unit level was superior to another in the prevention of rickets. Within the dosage range used for each type of antirachitic, the higher dosage levels appeared to be more effective. Advance in the rachitic process occurred most frequently in infants receiving cod-liver oil, least frequently in those given vitamin D milk Regression or healing of slight nickets tended to occur more promptly in infants receiving vitamin I) milk of the higher (400 units) dosage level than in those receiving that of the lower level (150 units). Of the different types of vitamin D milk containing 400 units, that to which viosterol was added appeared to be the most efficient. This form tended also to be more efficient than viosterol alone, even when the latter was given at a somewhat higher level In the final evaluation, it is sug-

gested that the value of a substance containing vitamin D should be measured first in terms of success in the prevention of rickets under practical conditions and, second, in terms of economy and that such economic considerations must include not only the cost of the vitamin but also the need and cost of other nutrients supplied by the vehicles carrying vitamin D.

A somewhat sımılar study has been conducted by T G H Drake 284 No differences were detected in the antirachitic effectiveness in human beings. rat unit for rat unit, of vitamin D administered in the form of cod-liver oil, of a mixture of fish liver oils of high potency (percomorph liver oil), of irradiated cholesterol, of irradiated fresh milk, or of irradiated evaporated milk No evidence was observed of any difference in the antirachitic effectiveness in human beings between the daily administrations of 150 USP units of vitamin D in the form of any of the above mentioned substances and that of 270 U S P units of vitamin D in the form of viosterol Since smaller amounts of viosterol were not administered, it was believed to be entirely possible that this substance is as effective in human beings, rat unit for rat unit, as are the others. The administration of vitamin D in amounts as low as 95 U S P units daily prevented the development of rickets of a moderate or marked degree in every instance Rapid healing of rickets of moderate or marked degree resulted from the daily administration of as little as 300 and 500 U S P units of vitamin D.

Similarly, J M Lewis²⁸⁵ found no differences, unit for unit, in the ability of cod-liver oil, viosterol, and percomorph liver oil to prevent rickets in infants. In respect to the curative effect of these three antirachitic agents as well as that of irradiated cholesterol, Lewis found

that the three antirachitics of animal origin (cod-liver oil, percomorph liver oil and irradiated cholesterol) were more effective, rat unit for rat unit, in the treatment of infantile rickets than was vitamin D of plant origin (viosterol).

The observations of T G H Drake. Tisdall and A Brown²⁸⁶ also F indicate that the antirachitic value of 150 international vitamin D units administered daily to infants in the form of irradiated cholesterol is equal or possibly slightly more effective than 150 international vitamin D units in the form of The daily administration cod-liver oil of this dosage of either irradiated cholesterol or cod-liver oil during five winter months was adequate to prevent the development of rickets of a moderate or marked degree in 151 normal infants.

According to D H. Shelling,287 the addition of viosterol to milk in the form of an emulsion enhances the efficacy of the viosterol about tenfold in curing moderate and severe degrees of rickets It is suggested that the increased potency of milk rendered antirachitic by direct irradiation by feeding vitamin D to the cow, or by the addition of vitamin D which ultimately becomes dispersed within the fat globules, is due to the small size of the lipoid particles in which the vitamin is carried, and hence is probably more easily absorbed from the gastroenteric tract. The advantages of producing vitamin D milk by the addition of viosterol to milk is an economical one since it offers a practical and cheap means of providing vitamin D in more effective amounts than is possible by direct irradiation or by feeding vitamin D to the cow.

L T Davidson, K K Merritt and S S Chipman²⁸⁸ have compared the antirachitic potency of irradiated evaporated milk with that of vitamin D milk from cows fed irradiated yeast. In their

experience, irradiated evaporated milk was considerably less efficacious for the protection of premature infants against rickets than was metabolized vitamin D milk, when the two were given under identical conditions The inferiority of the irradiated milk was believed to be due entirely to the smaller concentration of vitamin D acquired in the process of its production Full term infants, with one exception, were almost completely protected against all but the slightest roentgenological evidence of rickets This was in marked contrast to the more severe degree of rickets observed in the rapidly growing, premature infants.

Confirmatory data that irradiated yeast, when fed in adequate amounts, supplies sufficient vitamin D to prevent rickets in growing infants, are supplied by T G H Drake, F. F. Tisdall and A Brown 289 The daily administration for five winter months of approximately 500 international vitamin D units in the form of irradiated yeast to 69 normally growing infants prevented the development in each instance of rickets of a moderate or marked degree The daily administration of approximately 1000 international vitamin D units in the form of irradiated yeast to one infant with marked rickets and of approximately 500 units to four infants with moderate or marked rickets brought about definite healing in the course of one month

Clinical studies to determine the antirachitic potency of *crgosterol activated* by low velocity electrons have been carried out by I McQuarrie, W H Thompson, A V Stoesser and L G Rigler ²⁹⁰ The low velocity electron process is a new method for activating ergosterol and like the ultraviolet ray process can be employed on as large a scale as may be desired. The clinical studies indicate that this antirachitic is as active as cod-liver oil both as a prophylactic and as a cura-

tive agent. The average minimal preventive dose of ergosterol activated by means of low velocity electrons has not been definitely established. On the basis of their observations, it appears to be not above 300 U S. P vitamin D units per day for full term infants and 540 units per day for premature infants

G. Stearns, P C Jeans and V. Vandecar²⁹¹ have compared the rate of growth in length of infants given one teaspoonful of high grade cod-liver oil (340 to 400 U S P units of vitamin D daily) with that of infants given the same type of diet, but with the source of vitamin D from irradiated milk (60 to 135 USP units of vitamin D daily) or its vitamin D equivalent as cod-liver oil or cod-liver oil concentrate milk. The linear rate of growth in these two groups of infants was then compared with the standard growth rates reported in the literature The infants who received 340 to 400 U S P units of vitamin D daily increased in linear growth at a definitely more rapid rate than did those infants receiving 60 to 135 U S P units of vitamin D daily The latter group of infants grew at the same rate as the recently published standard rates Exposure to sunlight increased the rate of growth in the few infants in whom this measure was tried and who were receiving the lower of the two stated amounts of vitanin D. The authors are inclined to attribute this increased rate of linear growth to the increased intake of vitamin D with its resultant effect on skeletal growth They recognize, however, that the influence of vitamin A has not been entirely excluded in this group.

Studies in Mineral Balance

Iron retention in infants from various articles of diet has been studied by G. Stearns and D Stinger ²⁹² One infant was fed human milk, the others were

given a basal diet of cow's milk, carbohydrate and orange juice The daily iron intake was increased by giving egg yolk. spinach, a special cereal, or an iron salt The baby fed human milk was never in negative iron balance, although the retention was always small Those infants given cow's milk, alone, lost an average of 005 mg. of iron daily The age of the infant had no apparent influence upon the ability to retain iron Neither egg yolk nor spinach, in the amounts given, increased the iron retention. The retention of iron was definitely increased when the infants were given the special ironrich cereal or ferric ammonium citrate No consistent relationship was observed between the iron retention and the increase of potassium, calcium or phosphorus On the basis of their work, they conclude that an intake of 0.5 mg per kilogram of body weight is necessary to assure a retention of iron and that an intake of 1 to 15 mg per kilogram of body weight permits ample retention

Similar results were also obtained by F W Schlutz, M Morse and H Oldham ²⁹³ They found no increase of iron retention or increase of hemoglobin in three cases of secondary anemia when puréed spinach was added to the diet The iron of apricots, although utilized somewhat better than that of spinach, effected no change in hemoglobin and only a slight increase in retention. Iron salts, when given in large amounts, either in the form of ferrous sulfate or ferric ammonium citrate, caused a marked increase in the retention and a rise in hemoglobin They had no evidence that the ferrous salt was more efficacious than the ferric salt.

The effect of deficient mineral intake on intestinal activity has been studied by E C. Robertson ²⁹⁴ His experimental evidence indicates that diets low in minerals tend to reduce intestinal activity

and produce stasis Rats fed a diet low in minerals showed intestinal stasis, which was evidenced by dilatation and overloading of the large intestine and by definite delay in excretion. When calcium and potassium salts were added to the diet deficient in minerals practically no stasis occurred. Nineteen children were fed diets low in calcium and potassium and of these 14 became constipated When given a barium meal, 33 per cent of 18 children fed diets low in calcium and potassium retained the barium in the appendix for abnormally long periods (from 4 to 21 days) The same children, when fed normal diets, did not show barium in the appendix for more than one day.

PARASITIC DISEASES

By Waldo E Nelson, AB, MD

In a series of 220 necropsies, T B Magath²⁹⁵ found trichinae in samples of various muscles taken from 17 of Two gram samples were the bodies taken from the diaphragm, intercostal muscles, sternocleidomastoid and the The author believes rectus abdominis that if larger samples of muscle had been examined, trichinae would have been found in a greater number of bodies He estimates that from 10 to 20 per cent of the adult population have acquired trichinal Such data suggests that trichinosis may not only be incorrectly diagnosed but is probably often subclinical in intensity The need for evaluation of the skin and precipitin tests is pointed out

Strongyloides Stercoralis

Two instances of strongyloides ster-coralis infestation occurring in the temperate zone are reported by E A Wagner ²⁹⁶ It is pointed out that in the differential diagnosis of parasitic infestation, this parasite must be considered. In mild cases there may be no symptoms Diarrhea and epigastric distress are common. General malaise, anorexia, pallor, failure to gain in weight are frequently observed in children. In making the diagnosis, complete deviation tests and cutaneous reactions have been found to

be of little value As a rule there is an eosinophilia and a secondary anemia The diagnosis is confirmed by finding the rhabditiform larvae in the stools The ordinary cover slip preparation of a fresh stool will show actively motile larvae Confusion with hookworm is possible but as a rule the embryos of hookworm are in unhatched eggs and the hookworm has a much longer pre-esophygeal oral cavity The filariform larvae which occur in the hyperinfective form may be identified by their small size and minute terminal notch in the tail Gentian violet in $2\frac{1}{2}$ grain (0 162 Gm) enteric coated tablets appears to be the treatment of choice One tablet is given before each meal for a period of seven to ten days. In some instances two courses may be needed There are no contraindications to its use although mild nausea sometimes occurs

According to P D Lamson and C B Ward,²⁹⁷ the use of earthworms as a test for evaluating the activity of anthelmintics to be used in human intestinal helminth infestation is irrational. A comparative study of the lethality of 121 widely diversified chemical substances on both earthworms and pig ascaris showed no correlation. *In vitro* tests of human ascaricides on pig ascaris, which is morphologically indistinguishable from human ascaris, are of value

POISONING IN CHILDREN

By WALDO E NELSON

Lead

That lead which has been previously ingested and stored in the bones, may be liberated by changes in the body resulting from an acute infection and produce such manifestations of acute lead intoxication as encephalitis, is pointed out by R. E Netzley 298 Four instances of lead encephalitis which were initiated by such infections as otitis media, mastoiditis, tonsillitis and pertussis are reported The diagnosis of lead encephalitis was confirmed by the presence of basophilic stippling of the red cells, increased amounts of lead in the urine and lead lines in the roentgenograms of the long bones. The treatment suggested is that of replacing the lead in the bones in its original mert form and of doing nothing that would tend to hasten its liberation directed toward deleading the bones have resulted in the recuirence of cerebral Therefore, allowing sponsymptoms taneous elimination of the metal is probably the more satisfactory treatment

Changes in the growing skeleton after the administration of bismuth similar to the skeletal changes in lead poisoning are reported by J Caffey 299 The skeletal lesions due to lead and to bismuth are, in the author's opinion, roentgenologically identical. Such lesions were produced in the ends of bones of experimental animals by administration of bismuth. The chief anatomic change at the ends of the long bones was an excessive amount of calcificed cartilaginous matrix, and a corresponding decrease in narrow spaces The chemical analyses indicated that the actual bismuth content of the ends of the bones played a relatively minor rôle in the production of the radiographic shadow and that the calcium content of the compact cartilaginous matrix was from 9 to 17 times as important as bismuth in this respect. In similar lesions caused by lead, on the other hand, the extraneous metal is more significant

The author reports four types of lesions to illustrate bismuth changes which follow antisyphilitic therapy (1) The lesions which occur directly after a single course of treatment with bismuth (see Fig 1), (2) those which occur many weeks after a single course (see Fig 2), (3) those which occur after multiple courses during several years (see Fig 3), and (4) those which occur in newborns whose mothers received bismuth during pregnancy (see Figs 4 and 5)

Salicylate Poisoning

The danger of overdosage of salicylates has not been sufficiently stressed, and for this reason the report of B D Bowen, J F Roufa and O W Clinger,300 in which they point out the similarity of salicylate poisoning with diabetic or renal acidosis, is particularly timely diabetes in children may not be suspected until symptoms of acidosis appear, eirois in the differential diagnosis from salicylate poisoning may be made, unless blood sugar and carbon dioxide determinations are made Confusion may arise, particularly from the examination of urine The urine of patients who are taking salicylate reduces copper solution, often quite completely Furthermore, the Burgundy red reaction of aceto-acetic acid and the violet color produced by salicylate in the Gerhardt test may be confused Starvation under such circumstances may produce ketonuria (sodium nitroprusside test) When such an emergency exists, there is not time to differentiate the reducing substance of salicylate and dextrose in the urine by the fer-

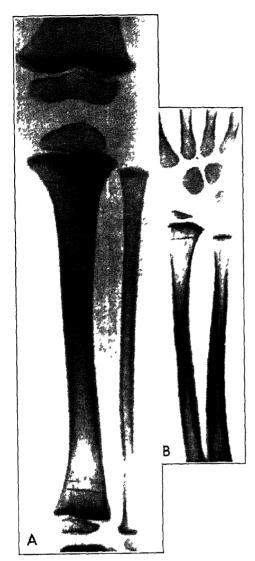


Fig 1—Heavy transverse bands of increased density at the ends of the shafts after a single course of treatment with bismuth (Courtesy, Amer J Diseases of Children, Jan, 1937)



Fig 2—Transverse bands deep in the shafts three and one-half months after a single course of treatment with bismuth (Courtes), Amer J Diseases of Children, Jan, 1937)

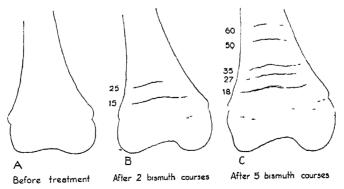


Fig 3—Multiple bismuth lines in the shafts after multiple courses of treatment with bismuth. The number opposite each line indicates the number of months which had elapsed since the administration of bismuth. (Courtesy, Amer. J. Diseases of Children, Jan, 1937.)

mentation method. The finding of the violet color reaction in the spinal fluid with ferric chloride may be a useful differential diagnostic procedure. Dyspnea is an important symptom of salicylate poisoning, and it is largely because of this hyperpnea that acidosis of diabetic or

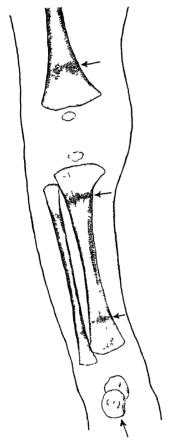


Fig 4—Bismuth lines in the newly born buried deep in the shafts tollowing treatment of the mother relatively early in pregnancy (Courtesy, Amer J. Diseases of Children, Jan., 1937.)

tenal origin is often suspected. The author's table, listing the comparative conditions found in diabetic acidosis and salicylate poisoning, is reproduced here

Three instances of salicylate poisoning in children are reported by K Dodd, A S Minot and J M Arena 301 Experimental work was also carried out by these authors to determine the explana-

tion of the more serious manifestations of poisoning by this drug They state that the administration of salicylate causes a prompt increase in both production and elimination of heat No serious symptoms are produced by the administrations of large amounts of salicylate to an experimental subject as long as the intake of fluids is adequate and there is no interference with the processes of the elimination of heat. When the ability to dissipate heat is experimentally interfered with, otherwise harmless doses of the drug cause death as a result of hyperpyrexia and exhaustion tients, when dehydration causes a similar mability to adapt themselves to the action of the drug, alarming symptoms of salicylate poisoning develop Treatment of salicylate intoxication should place emphasis first on the administration of large amounts of fluids, together with other measures to aid in the dissipation of heat. Later in the intoxication, when acidosis is often present, alkalı should also be given Food, if it can be retained, or dextrose administered parenterally, should be furnished as rapidly as is feasible in order that excessive catabolism of body tissue may be avoided and ketosis guarded against

Carbon Tetrachloride Poisoning

In instance of carbon tetrachloride porsoning (noninflammable cleaning fluid, energine) in an infant two years of age is reported by H L Heyl 302. The author's outline of treatment is as follows (1) Emergency gastric lavage, catharsis; (2) low fat, low protein, high carbohydrate diet, (3) calcium intake maintained at 0.5 Gm intravenously, or 2.0 Gm by mouth daily (15 grains or 1 Gm of calcium is contained in 1000 cc of milk, in 150 grains or 10 Gm of calcium gluconate, in 60 grains or 4 Gm of calcium lactate, or in 45 grains or

3 Gm of calcium chloride); (4) if vomiting is marked, continuous intravenous drip with calcium gluconate, five per cent glucose and normal saline should be administered, (5) parenteral fluids and transfusion as indicated, and (6) studies of blood sugar, CO₂, nonprotein nitrogen, calcium, serum protein, fat, guanidine and lactic acid

antitoxin The authors point out that botulism and mushroom poisoning (mycetismus) should not be confused clinically Their summary of the clinical course of poisoning from each of these substances is as follows: "The onset of symptoms in botulism only rarely occurs earlier than 12 hours after ingestion of the toxin, and the symptoms in order of

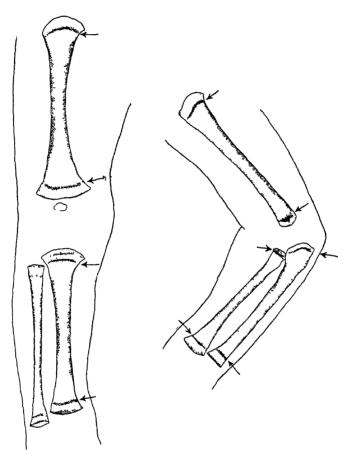


Fig 5—Bismuth lines in the newly born near the ends of the shafts following treatment of the mother late in pregnancy (Courtes, Amer J Diseases of Children, Jan, 1937)

Botulism

The death of two children from botulism caused by eating home-canned wild mushrooms is reported by R B Lindsay, J R Newnam and I C Hall ³⁰³ The fact that the lives of the parents were saved was attributed to the possibility of a weak toxin and the timely prophylactic administration of botulinus

appearance are diplopia and dilatation of the pupils with dimness of vision, vertigo, aphonia, muscular weakness, dysuria, constipation, salivation due to strangulation and respiratory failure. Nausea, abdominal cramps and voniting occur occasionally, but diarrhea rarely, if ever, occurs Terminal convulsions may be observed occasionally but never early in the dis-

TABLE 1

Comparative Conditions Found in Diabetic Acidosis and Salicylate Poisoning*

| | Diabetic Acidosis | Salicylate Poisoning |
|---|---|--|
| Symptoms and Signs Onset Epigastric Vomiting Hyperpnea Dehydration Thirst Coma Hypotension | Slow May be present Usually present Present Present Present May be present May be present | Rather slow May be present Usually present Present Present Present May be present May be present |
| Laboratory Examinations Blood Sugar CO2 capacity Leukocytes Polymorphonuclears Urine Albumin Casts Red blood cells Copper reduction (dextrose) Ferric chloride Sodium nitroprusside Spinal fluid Pressure Ferric chloride | High Low May be increased May be increased Present Present May be present True Burgundy red Present Probably normal May be positive | Usually normal Slightly decreased May be increased May be increased Present Present May be present False Violet May be present May be increased Violet (false) |

^{*} The following are rarely seen in diabetic acidosis but frequently in salicylate poisoning tinnitus, twitching, convulsions, deafness, dimness of vision, sweating, hallucinations, disorientation, delirium and urticaria

ease Patients suffering from botulism generally remain conscious until a few seconds before they die, and the heart is often observed to beat a few seconds after respiration ceases, * * * The mortality is high, between 60 and 80 per cent

Mycetismus (Mushroom Poisoning)

"Mycetismus (mushroom poisoning) may be discussed briefly under five headings, as proposed by Ford 304

"In mycetismus gastrointestinalis caused by certain species of lactarius, entoloma and lepiota, all the symptoms are limited to nausea, abdominal cramps of variable intensity, vomiting and diarrhea Neural symptoms never occur, and the mortality is low. There is no danger of confusion with botulism, but similar symptoms might be caused by other

forms of food poisoning, notably those due to the staphylococcus, bacterium paratyphosum or bacterium enteritidis

"In mycetismus chloreiformis, which is caused by Amanita phalloides and probably also by pholiota autumnalis and hygrophorus conicus, the onset is generally characterized in from 10 to 15 hours by violent abdominal cramps, nausea, voiniting and diarrhea, rapidly followed by loss of strength, the appearance of casts in the urine due to damaged kidneys, and heart failure. Liver function is also impaired. The mortality is high, about 50 per cent. Neural symptoms are absent and there is little danger of confusion with botulism.

"In mycetismus nervosus, which is due to those mushrooms containing muscarin, such as amanita muscaria, amanita pantherina and certain species of inocybe and clitocybe, violent gastrointestinal symptoms may appear within two or three hours, accompanied by contracted pupils, profuse perspiration and salivation, localized or generalized convulsions, delirium, hallucinations and death in coma with acute dilatation of the heart. Unless treated early with atropine, the mortality is high. There is little danger of confusion with botulism

"In mycetismus sanguinareus, caused by helvella esculenta, the outstanding symptoms are hemoglobinuria and abdominal distress followed by a mild persistent jaundice. The mortality is low and confusion with botulism should never

"The last form of mushroom poisoning, mycetismus cerebralis, caused by certain species of panaeolus, is possibly the only one likely to be confused with botulism because of the disturbances of vision and the staggering gait. However, the earlier onset, from four to five hours, the exhilarating intoxication and the low mortality should serve clearly to distinguish it from botulism"

POLIOMYELITIS (INFANTILE PARALYSIS)

By ROBERT A LYON, AB, AM, MD

Epidemiology-In spite of epidemics of poliomyelitis which occur from time to time, usually more severely in the seaboard states than in the interior of the United States, the disease does not attack a large number of people J P Leake³⁰⁵ has stated that the total number of deaths from poliomyelitis averaged 800 a year in the registration area for the three-year period 1933 to 1935 The number of persons affected by paralysis has been estimated at ten per 100,000 population Whether or not the infection is contracted from carriers, insects or by way of the gastro-enteric tract has not been determined. In some past epidemics it has been shown that the disease has not been spread in swimming pools and beaches. It still seems wise, however, for an individual to stay away from unnecessary contacts during an epidemic and to avoid over-fatigue and exertion which has seemed to play some part in increasing one's susceptibility to the disease The accurate reporting of all forms of infantile paralysis is a necessary step towards the determination of etiologic factors

Pathology—An important portal of entry of the poliomyelitis virus seems to be the nose and olfactory bulb The work of A B Sabin and P K Olitsky306 has demonstrated pathologic changes in this locality in rhesus monkeys which had received nasal instillations of 10 cc of a ten per cent virus suspension on two occasions, 48 hours apart The lesions first occurred on the fourth day after the administration of virus and slowly invaded the rest of the brain but the spinal cord involvement and the paralysis did not occur for four more days. Often only one olfactory bulb was affected so that the necessity of examining both sides was emphasized

Immune or convalescent rhesus monkeys were resistant to second nasal instillations of the virus as far as pathologic changes in the olfactory bulbs were concerned. When the virus was introduced by other routes, the disease occurred without the olfactory pathway

being involved which indicated that other nerve pathways may be the means of conveying the infection. Autopsy reports of human cases of poliomyelitis have shown normal olfactory bulbs in many instances and the authors believed that the virus may invade man in a manner quite different from that in experimental animals.

That the virus of poliomyelitis travels chiefly by way of the channels within the neuraxis has been substantiated by the studies of J A Luhan 307 After intracerebral injection, the virus did not follow any definite pathway down the brain stem but was generally found to course through the channels of the decussating fibers The cerebrospinal fluid did not carry the virus and the involvement of the meninges was always minimal Perivascular infiltration with blood cells, chiefly of the polymorphonuclear and lymphocytic types was one of the first lesions to be noticed in the brain The polymorphonuclears soon underwent fragmentation and degeneration and were replaced by microglial It seemed possible, from these studies, that the virus might spread throughout brain tissue by continuity and that occasionally the virus might be picked up by the blood stream and disseminated throughout the neuraxis in this fashion. The mesenteric and intestinal lymph nodes were frequently enlarged, and in one instance the thyroid and liver had definite infiltrative changes suggesting an occasional localization of the virus in other organs than the central nervous system

Recent experiments made by J A Toomey³⁰⁸ have convinced him that poliomyelitis symptoms develop in monkeys more rapidly when the virus is combined with toxic material resulting from intestinal stasis. When the pathways between the spinal cord and in-

testinal tract were blocked by the injection of alcohol into the superior and inferior mesenteric nerves and poliomyelitis virus was injected into the cerebrum of rhesus monkeys, the symptoms of the disease were delayed in their appearance for several days. When monkeys were prepared in advance by the injection of alcohol into mesenteric nerves, intestinal stasis developed, toxic enteric products increased in quantity in the stools and in the blood so that the subsequent intracerebral injection of poliomyelitis virus was followed by the rapid development of paralysis

The absorption of the virus of polioinvelitis from the intestinal tract and the conveyance of it to the central nervous system by way of the mesenteric nerves and possibly also the vagus nerve have been demonstrated in rhesus monkeys by J A Toomey 309 The pathologic changes occurring in such animals have been examined at various intervals of time after the virus had been inoculated into the subserous layers of the gut Within 24 hours after the injection, changes in structure of the lumbar region of the cord occurred Destruction of cells of the spinal ganglia was first noted, later the motor cells of the cord and anterior horn and then the cells of the posterior column were af-The meninges rarely showed more than local areas of inflammation Occasionally the pons became involved before the thoracic or cervical portions of the cord, which indicated to the author the probability that the virus ascended the vagus nerve as well as through the lumbar sympathetic system After the motor cells were destroyed, a rapid proliferation of neuroglia occurred and three to five days later there was a perivascular infiltration of round cells but never with polymorphonuclear types Occasionally death occurred before the vascular reaction took place but the presence of the latter often aggravated the amount of edema and destruction.

As a rule the virus of poliomyelitis travels along nerve pathways without causing destruction Thus the intracerebral injections of virus are followed by its migration for considerable distance before symptoms occur J. A. Toomey and H M Weaver³¹⁰ injected the virus into the subserous lavers of the intestinal tract there was evidence that the nerve fibers received immediate damage before the infection reached the cord This early peripheral nerve damage suggested to the authors the possibility that cases of so-called bulbar poliomyelitis in which no pathologic changes can be detected in the brain might be produced by vagus degeneration caused by the immediate effect of the virus in its course along that nerve from intestinal routes of infection

The possibility that the barrier between the blood stream and central nervous system might be more readily permeated in poliomyelitis, as is the case in meningitis, has been disproved by P H Harmon and W M Krigsten 311 They employed four materials to test this permeability and in no instance did the dyes pass more readily from the blood into the brain in animals with poliomyelitis than in a normal control The authors suggested that standardized tests of this nature might be employed to differentiate poliomyelitis from such infections as tuberculous meningitis in which the barrier is reduced in permeability

Diagnosis—The isolation of the poliomyelitis virus from the nasal secretions of patients has been a difficult matter A method has been described by S D Kramer, A E Sobel, L H Grossman and B Hoskwith³¹² which employs a vacuum desiccation technic from frozen nasal washings. The concentrated material obtained in this fashion from two patients with poliomyelitis on the thirteenth and sixteenth days of the disease produced typical poliomyelitis in rhesus monkeys when injected intracerebrally.

Attention has been called to the difficulty of making the diagnosis of nonparalytic poliomyelitis, and especially in differentiating it from choriomeningitis P. F. Lucchesi313 reported a recent epidemic in Philadelphia consisting of 67 cases with symptoms of either disease About one-half of the group had evidence of weakness or paralysis of muscles and were considered to be true cases of poliomyelitis The remainder had symptoms of fever, headache, nausea and vomiting, pain and stiffness of the neck or back. All had some increase in the number of lymphocytes in the cerebrospinal fluid The absence of paralysis, however, made the author consider the possibility of another type of disease The need for a more simple laboratory or clinical test to differentiate poliomyelitis from other diseases of the choriomeningitis type was emphasized

Second Attack—Immunity to poliomyelitis has seemed to be a relative matter and second attacks of the disease are theoretically possible J A Toomey³¹⁴ was able to produce symptoms of paralysis by the injection of large doses of the virus in all but eight of a group of 18 monkeys which had had the disease previously. The eight animals which escaped paralysis with the second injection had had severe symptoms of quadriplegia during the first infection. Those which developed second attacks had had milder symptoms with their primary poliomyelitis.

The problem of second attacks of poliomyelitis has been investigated also by S Flexner ³¹⁵ A group of 27 ani-

mals, which had had the infection previously, succumbed to second attacks when virus was introduced by the nasal route After a quiescent period of some months, another dose of virus was instilled into the noses of some but no third attacks could be produced, although an increase in cells in the cerebrospinal fluid sometimes occurred A severe initial attack did not seem to be any more security against a second infection than did mild The quantity of preliminary attacks neutralizing substance in the blood was no indication of an animal's response to a second infection Not all strains of virus were equally effective in producing second infections and whether or not it was the same strain of virus as produced the initial attack seemed unimportant The author was inclined to believe that man might suffer second attacks or numerous attacks of a mild nature without exhibiting clinical evidence of the disease.

Complications—Severe nephritis following poliomyelitis seemed to be mainly responsible for the death of a patient observed by B L Keyes 316 A 13-year-old boy contracted poliomyelitis which resulted in paralysis of the muscles of the arms, legs, trunk, neck, and of the muscles of respiration so that he was placed in a Drinker-Collins respirator On the fourth day of the illness, improvement in respiration took place and the temperature dropped to almost A gradual return of function in some muscle groups was noted during the following days but urinary retention and occasional hematuric episodes occurred The blood pressure was elevated throughout the illness and after two months, nausea, vomiting, dimness of vision developed and the patient died in a convulsion The autopsy revealed an ascending pyelitis and a severe tubu-

lar nephritis with hemorrhage in the collecting tubules.

Immunity—The factors which may render an individual immune or susceptible to poliomyelitis have been reviewed recently by W L Aycock 317 Although the portal of entry of the virus seems to have been established as the nasal mucous membranes, there is some doubt whether this is the only route or whether the permeability in this area determines immunity or susceptibility Employing nasal sprays of one and four per cent alum solutions, tannic acid, and picric acid in successive experiments, he was able to protect monkeys temporarily against nasal instillations of the virus However, questions were raised whether man was ever exposed to such large amounts of virus and whether some human subjects did not have a very great susceptibulty such as might not occur in monkeys and might not be prevented by nasal blockage Since most individuals seem to develop an immunity from subclinical attacks of the illness, the blockage of the nasal membranes might be considered to be disadvantageous

A review of other contributing factors indicated some evidence that certain families were especially susceptible and that certain familial endocrine variations might be more prevalent among poliomyelitis patients. Anthropometric determinations have shown that persons of pituitary gonadal imbalance are slightly more susceptible. Castrated female monkeys and those receiving injections of estrin developed the infection in greater proportions than normal control animals.

The action of *vitamin C* in neutralizing poliomyelitis virus has suggested that it might be of value to a patient in the development of immunity against the disease. In the studies made by C W Jungeblut³¹⁸ about 100 rhesus monkeys

were given vitamin C in different doses before or after intracerebral injection of poliomyelitis virus. The administration of about 5 mg. of crystalline vitamin C seemed to reduce the incidence of paralysis by about one-half as compared with a control group. Larger doses of the vitamin or its administration before infection as a prophylactic produced no definite results. It appeared to the author that vitamin C might supply a factor which aided the natural resistance of the body to disease, a factor already shown to be of some importance in the case of diphtheria infections.

The part played by *vitamin D* in protecting an animal against poliomyelitis has been investigated by J A Toomey. 819
The administration of vitamin D protected rhesus monkeys from the infection when the virus was introduced by way of the intestinal tract and the lack of vitamin D seemed to make animals more susceptible to similar infections. However, the fact that poliomyelitis is most frequently epidemic during warmer summer months when the vitamin D supplied by sunshine is greatest, seemed paradoxical to the author.

A relationship between the resistance and susceptibility of a patient to poliomyelitis and diphtheria has been suggested by C W Jungeblut 320 The sera of horses and monkeys which have been immunized against diphtheria have occasionally contained neutralizing substances for the poliomyelitis virus and these animals have demonstrated an increased resistance to infection with the virus No relationship, however, was found between the antitoxin concentration and the amount of poliocidal bodies clinical viewpoint, several observations have been made in the past of the increased frequency of positive Schick reactions in patients with poliomyelitis A limited amount of data has been collected which indicated that children contracting poliomyelitis were also susceptible to attacks of diphtheria. From these several observations, the suggestion was made that a nonspecific resistance to both diseases might occur, which required further investigation.

A substance which neutralizes poliomyelitis virus has been found in the blood of normal individuals, convalescent patients and in that of animals which have had the disease or have been treated with It is the opinion of J. A. vaccines Kolmer³²¹ that this neutralizing substance may be classified as an antibody similar in many respects to an antitoxin From a review of the investigations of the potency of various blood sera in producing passive immunity, the author concluded that the amount of antibody in human or experimental animals was much greater in those who had recently recovered from the disease than in normal ones Antibodies may be built up by vaccination in amounts which may be sufficient to provide protection administration of serum to patients with the disease must be in large doses if it is expected to be adequate for protection At least 5 cc of protective serum should be administered per kilo of body weight The time factor is also important because convalescent serum will not neutralize virus which has already invaded a cell and, therefore, it must be given at least two days after the first symptoms of the disease If it is given after paralysis has set in, the only beneficial results to be expected are the prevention of further involvement of the nervous system

The value of *vaccination* by virus, treated with sodium ricinoleate, has been proved in animal experimentation. The author employed five successive doses of 0.1 to 0.5 cc administered subcutaneously or intracutaneously every five days. All animals resisted virus which was

injected intracerebrally two weeks after the immunization. In the blood of these monkeys were poliomyelitis antibodies. Following numerous injections of vaccine, children will also produce amounts of antibody in their blood which are equal to that found in the blood of convalescent patients. It seemed to the author that the presence of adequate amounts of antibody in the blood will protect an individual, regardless of the portal of entry of the virus.

The significance of antibodies of poliomyelitis in the blood stream has been doubted by P H Harmon and H N. Harkins 322 The immunity of individuals apparently varies considerably Second attacks of the disease have been observed in 17 instances during the past 20 vears' experience with poliomyelitis in the United States and Canada examination of the blood of 183 convalescent patients has demonstrated the virus neutralizing substances to be absent in about 40 per cent of the total number The percentage of negative results in different groups has varied between 12 to 64 and the examination of normal individuals of different ages without history of contact or infection has indicated that the neutralizing substances developed in higher percentages in such groups than among convalescents Children under five years of age had antibodies in 37 per cent of instances while those of 15 years had such immunity in 73 per cent of cases

The mechanism responsible for antibody development is not known definitely but it seems likely that direct contact of the individual with the virus is necessary. An examination of a series of the blood antibodies of 14 patients convalescing from the disease gave varying results. One individual developed paralysis 24 hours after his blood was shown to have a high titer of antibodies. Others with small antibody content did not develop severe paralysis Seven of the group had received human convalescent serum but in only one instance had the quantity of neutralizing substances risen to any great extent. A series of animal experiments along similar lines also gave a variety of results so that the authors were led to conclude that evidence of the mechanism of action of human convalescent serum used to prevent or to combat poliomye-They favor furlitis is entirely lacking ther trial of this method of treatment. however, since favorable clinical results have been reported in many instances

The resistance of vaccinated and of convalescent monkeys to intranasal instillations of virus has been investigated by A B Sabın and P K Olıtsky 323 None of a group of nine convalescent rhesus monkeys could be reinfected by nasal instillations of virus, even though the amounts of neutralizing substance in their blood were low at the time of testing Vaccinated monkeys may be infected by the nasal route even though their serum antibody content seems adequate The experiments seemed to indicate that the quantity of circulating antibody does not determine the status of an individual's immunity

The opportunity to observe the occurrence and development of neutralizing substances in the blood sera of 82 paralytic, 32 nonparalytic and three encephalitis patients throughout course of their disease was offered to M Brodie, A E Fischer and M Stillerman 324 There was a total lack of uniformity in the results obtained As many as 50 per cent of the patients, tested during preparalytic stages or during the height of the infection, possessed neutralizing substances Only very small percentages of those who did not have antibodies before or during the paralytic stages developed this protection during the following 12 to 14 months. Three patients had even lost the neutralizing material which had been present at the beginning of the infection when they were examined two months or more later. The authors were forced to conclude that no relationship could be established between the presence of neutralizing substances in the blood serum of an individual and his resistance to the disease, nor was the antibody content of any value in determining the diagnosis of nonparalytic forms of infection or in prognosing the degree of recovery

A survey of the potency of convalescent poliomyelitis serum was undertaken last year in Denmark, following a rather severe epidemic of the disease which had occurred in 1934. The results have been reported by G H Eagles, C Jensen and E J Henningsen 325 The serum specimens were collected from three types of patients, the paralytic, the nonparalytic and the abortive cases potency of the serum was compared in neutralization tests with standard doses of virus consisting of 1000 times the minimal amounts necessary to produce paralysis in susceptible monkeys pooled lots of serum collected within 13 to 29 days after the disease did not seem to contain greater neutralizing power than that collected four months after the onset of the infection Considerable variation in potency of individual serums occurred In a limited number of tests it seemed that the pooled serum of normal adults compared favorably in antibody content with convalescent serum hyperimmunization of horses produced a serum equal or only slightly increased in potency over that of convalescents, but because of the dangers associated with the administration of horse serum, the human types seemed preferable Although the efficacy of serum administration in the treatment of the disease is not well established, it is necessary in further experimentation to test the potency of that which is administered. Pooling of samples will usually eliminate the chances of giving material low in neutralizing titer. Even pools of serum which test low may be concentrated to obtain the pseudoglobulin fraction which contains most of the antibody. The authors urged the establishment of an international standard to be employed in the testing of the potency of convalescent serum

Poliomyelitis antibodies could be recovered from the nasal washings of patients convalescent from the disease and from normal individuals by B F Howitt 326 Substances which would neutralize the virus were obtained from about 23 per cent of a group of 61 persons The blood serums of this group contained antibodies in 59 per cent of instances There was no definite correlation between these two findings, however, since only 64 per cent of those with positive evidence of antibodies in the nasal secretions had positive blood se-In 27 patients the serum was positive and the nasal secretion negative Positive results were obtained with slightly greater frequency in the normal adults and children than in convalescent The significance of the virucidal substances in the nose and in the blood, as well as the similarity in their nature, remained to be explained

Active Immunization — Additional animal experimentation with incinoleated vaccine to determine its effectiveness in producing an active immunity has been carried out recently by J. A. Kolmer 327. The vaccine employed consisted of a four per cent virus obtained from monkey spinal cords to which one per cent sodium ricinoleate and 1.80,000 phenyl mercuric nitrate had been added. The latter drug acted as a preventative against bacterial growth. The material was al-

lowed to stand for ten days at a temperature of 392° to 464° F (4° to 8° C.). When a group of 80 rhesus monkeys were given five to ten subcutaneous injections of this material in doses of 005 to 10 cc, immunity developed in 60 to 100 per cent, depending upon the dosage. A few developed paralysis during the immunization When the vaccine was administered intracutaneously in doses of 005 to 05 cc, none of the animals developed paralysis and 77 per cent had subsequent evidence of immunity It was the author's opinion that the intracutaneous procedure was a safer and more effective method of inducing active immunity than the subcutaneous method The presence of live, attenuated virus in the vaccine seemed to be necessary for the stimulation of antibody production and the dosage had to be sufficiently large to produce adequate protection

A series of experiments have been performed recently to test the relative antigenic value of various types of treated poliomyelitis virus S D Kramer³²⁸ was unable to find sufficient antibody response to the injection of 5 cc of a ten per cent suspension of virus treated with 0.1 per cent formalin as recommended by Brodie Neither animals nor children responded in adequate numbers with the development of neutralizing substances in their blood. With increased dosage, about 30 per cent of animals developed antibodies.

Immunization of rhesus monkeys by subcutaneous or intracutaneous injections of neutralized mixtures of virus and blood serum proved to be a safe procedure and led to antibody formation in considerable quantities, but not as great as resulted from a paralytic attack of the disease itself. This mixture, however, seemed to be as effective and more safe than the formalized virus antigen or the ricinoleated vaccine recommended by Kol-

mer which S D Kramer and L H Grossman³²⁹ found effective in only about 50 per cent of animals tested

Employing a purified virus adsorbed on aluminum hydroxide, S. D. Kramer, L H Grossman and B. Hoskwith³³⁰ were able to produce a satisfactory antibody response in rhesus monkeys The substance was injected subcutaneously in three doses of 5 cc at weekly intervals An equivalent of 15 grains (0097 Gm) of virus was administered in this manner and seven of a series of ten animals developed a satisfactory antibody content With larger doses, eight of ten experimental monkeys developed immunity levels of neutralizing substances in their blood The procedure seemed safe and the absorption of the material by the patient was slow, which is a factor which has often proved advantageous in the production of immunity to other diseases

Prevention—Assuming that the olfactory pathway is the chief route of virus invasion of the body, efforts have been made to find a substance which would protect the nasal mucous membrane or develop local neutralizing bodies Various chemicals have been employed as nasal sprays Zinc sulfate has proved the most satisfactory to E W Schultz and L P Gebhardt 331 A one per cent solution of zinc sulfate in physiological saline solution (09 per cent NaCl) sprayed into the noses of monkeys daily for three days has protected the majority of the animals against subsequent nasal instillations of virus A local anesthetic consisting of 0.5 per cent pontocame has been added to the spray recently, to reduce local nasal irritation and it has not seemed to interfere with the beneficial action of the zinc sulfate In order to determine the usefulness of this type of preventive treatment in a field study of human reactions, a long time program of experimentation will be necessary with accurate recording and estimation of results.

Surgical pituitrin S has been employed in doses of 05 cc as a nasal spray and has been followed with the instillation of 10 cc of adrephine which is a mixture of adrenalin and ephedrine with a small amount of chloretone Protection against poliomyelitis virus was established in animals by this procedure S D Kramer, L H Grossman and G C Parker³³² instilled these solutions into the nostrils of monkeys twice a day for five to seven days Poliomyelitis virus was dropped into the nose 12 to 96 hours later and the animals treated in this manner resisted infection and developed antibodies in their blood stream in greater proportions than did a control group The superficial and submucosal layers of the nose became infiltrated with large numbers of eosinophils

Nasal sprays are effective in affording protection against the poliomyelitis virus, only when they are sufficiently acid in reaction to cause the coagulation of proteins, according to the report of C Armstrong and W T Harrison 333 Solutions of picric acid which were buffered at a pH range which did not cause coagulation did not give adequate protection to animals, while buffer solutions alone, with an acidity of pH 28 or more, were only slightly better The most effective solution seemed to be one which would cause the prompt coagulation of proteins and these conditions were met best by a mixture of sodium aluminum sulfate and The forpicric acid in saline solutions mula for such nasal sprays consisted of 1 gram of sodium alum, dissolved in 100 cc of physiologic saline (085 per cent) added in equal parts to a solution of 1 gram of pieric acid on 100 cc of physiologic saline This formed a stable solution which might be used once every other day for four or five applications and then once a week for the duration of a poliomyelitis epidemic

The clinical use of such nasal sprays for the prevention of poliomyelitis during the past year has thrown some doubt upon their effectiveness as chemical agents or as a method which can be used with success by the laity. The survey reported by C Armstrong³³⁴ was conducted in Birmingham, Alabama, and the surrounding territory. During an

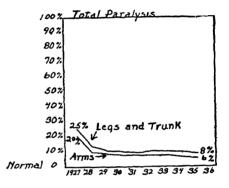


Chart 1—Yearly percentage of involvement in 53 cases of paralysis of the legs, arms and trunk (Courtesy, Jour A. M A, Aug 29, 1936)

epidemic, the preventive treatment was popularized through the press and the pierie acid-alum spray was administered by physicians in their offices, or the patients were instructed in its use at home Spraying every other day for one week and then once a week for the duration of the epidemic was recommended A house-to-house canvas of a sample of the population indicated that approximately 160,000 persons did not employ the treatment and about 270,000 did The very young and very old were sprayed less than other age groups. The incidence of poliomyelitis in this area among the treated group and among the untreated was in a ratio of 16 to 217 Among the causes of the ineffective use of the sprays were poorly operating spraying apparatuses, insufficient or indifferent spraying and the improper direction of the spray Children often resisted the treatments, so that the solutions frequently failed to reach the nasal mucous membranes in adequate amounts. Irritation from the solution decreased the number of sprays and amount of each treatment

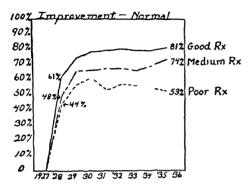


Chart 2—Yearly percentage of improvement in paralysis of the legs and trunk with good medium and poor treatment (Courtesv Jour A M A Aug 29 1936)

In some instances, sensitivity reactions occurred, none of which were serious but usually consisted of urticarial eruptions. Two cases of acute nephritis with hematuria were reported following the use of the sprays. The author concluded that the method was open to question as a general procedure until a more suitable and uniform means of instilling the solution was discovered and possibly until a better protective agent could be found.

Treatment—(For discussions of the value of convalescent serum in the treatment of poliomyelitis, see paragraphs under the heading of "Immunity")

The late results of treatment of 63 patients with poliomyelitis with the *respirator* (Drinker) have been analyzed recently by M B Brahdy 335 This group represented four per cent of the total number of poliomyelitis cases which were admitted to the Willard Parker Hospital over a three-year period from 1931 through 1933 Only those with severe res-

piratory difficulty, restlessness or cyanosis received treatment in the respirator Twelve patients had bulbar infections and all of them died Of the remaining 51 patients with spinal lesions with impaired intercostal and diaphragmatic action, 24 died, a mortality rate of 47 per cent Of the 27 survivors, 13 died 19 days to 4½ years later The most common cause of death was pneumonia, but pulmonary edema and neutropenia caused death in one instance each. The children usually had symptoms of cough and respiratory infection, followed by sudden dyspnea and cyanosis The roentgenograms of two patients showed massive atelectasis in one instance and pneumothorax in the other and the authors were inclined to believe that atelectasis might be a common complication of respiratory types of poliomyelitis, as a result of excessive bronchial secretion and the inability to expel it Only by roentgenograms can the accurate differentiation of this condition be made

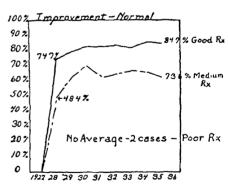


Chart 3—Yearly percentage of improvement of the arms with good and medium treatment (Courtesy, Jour A M A, Aug 29, 1936)

There were 14 patients who have survived a number of years after their initial respiratory involvement. One-half of the group were still considerably incapacitated by their paralysis but three of the group had good respiratory function. One other underwent an anesthesia for

an appendectomy without untoward results. The seven patients who were up and about had good respiratory function. The general results seemed somewhat discouraging but the authors believed that the respirator had been of distinct value to a small percentage of the total group and that further observation for the prevention of late respiratory disease might be an essential part in improving the end results following paralysis of muscles of respiration.

The necessity of continuous after-treatment and observation of postpoliomyelitis patients with paralysis, has been emphasized by A T Legg 336 Immediate treatment after the disease begins consists of the immobilization and splinting of the affected muscles to prevent stretching or contraction As soon as sensitiveness of the patient has been relieved with the aid of wet packs, warm baths and dry heat, the treatment of muscle training and physical therapy should be started and continued under the physician's observation Underwater treatment was considered very beneficial in furnishing buovancy to the

patient and thus stimulating his interest and activity. Most important of all are frequent examinations to determine the amount of improvement of muscle function so that the necessary changes of the type of exercises may be instituted The author made it his practice to examine each patient once a month for four months, every two months for two examinations, every four months for the next five years and then once every six months. A group of 53 patients who had been observed in clinics during a period of eight years were divided into groups which had attended with varying regularity and had, therefore, received good, medium or poor treatment differences in results occurred as have been represented in graphic form in the accompanying charts

Although the most striking improvement occurred in the first year after the disease, the gradual increases of muscle power which developed over a period of eight years indicated the necessity of careful follow-up and observation over a long period of time

THE RESPIRATORY SYSTEM

By Waldo E Nelson, AB, MD

Pneumonia

A method for rapid typing of pneumonococci is described on pages 643 and 644 in the 1937 Service Volume and the technic for obtaining gastric contents to secure material for typing on page 644. A preliminary report on the treatment of lobar pneumonia by artificial pneumothorax is reviewed on pages 645 and 646. The hypothesis of Miller and coworkers that allergic reactions within the lung may simulate pneumonococci is described on pages 645.

monia both clinically and roentgenologically is presented on page 647

Tonsils

Observations before and at intervals of two years after tonsillectomy and adenoidectomy have been made on 540 children between the ages of 2 and 13 years by I M Epstein 337 In general the observations of this author indicate better results from this operation than do the results quoted in other recent

reports It is stated, however, that better results may be expected if the tonsillectomy and adenoidectomy is postponed until the child is six years of age or older, especially if a head cold or cough is the complaint Except in the estimation of mechanical obstruction, the appearance of the tonsils is unimportant in determining the advisability of operation Large tonsils were almost always infected Buried tonsils did not differ histologically from others Redness of the anterior pillars was not a reliable indication of infection Tonsils which were cryptic usually contained more caseous material and tonsils with much caseous material almost invariably had cryptic abscesses No correlation was found between the types or degrees of tonsillar infection and the type or severity of preoperative symptoms, or the result of the operation Whether the tonsils were buried, cryptic, smooth, large or small, bore no relation to the preoperative symptoms or to the degree of success of the operation Very good results were obtained with children of all ages in the relief of sore throats and of cervical adenitis, good results in the relief of mouth breathing, fairly good results in the relief of cough, and fair results in the relief of frequent head colds.

Hemorrhage from Pharynx—Four instances of severe arterial hemorrhage from the pharynv secondary to retropharyngeal and parapharyngeal infections have been reported by I Frank and A F Abt 338 All of the children had had their tonsils removed several years previously. The hemorrhages occurred as a result of erosion of important arteries due to pharyngeal infection and were not due to injury or incision of blood vessels as a direct result of surgical procedure. Severe arterial hemorrhage as a complication of pharyngeal

infection, while not common, is usually of such sudden and dramatic occurrence that prompt and effective treatment is necessary Any of the arteries in the proximity of the affected area may be involved The internal carotid artery, because of its anatomical position, is Less frequently most often involved one of the branches of the external carotid artery is affected, such as the ascending pharyngeal or the ascending palatine arteries When the bleeding is from a branch of the external carotid artery, its ligation is advised. If the perforation is of the internal carotid artery, or of one of its branches, the carotid sheath should be exposed and the common carotid artery ligated on the affected side It must be understood that ligation of the common artery is not without danger, but the desperate situation permits no other choice the authors' cases, the common carotid artery was ligated in three instances, and the external carotid artery in one There were no resulting complications and the authors were convinced that the procedure was a life saving measure

Sinus Disease

In a study of a group of children with repeated upper respiratory infections, C G Kerley³³⁹ noted that accessory sinus disease was present in a high percentage of them. In his series of 504 children, 380 or 75 per cent had 10entgenologic evidence of sinus involve-In the care of these children. Kerley emphasizes the importance of paying attention to the general care of the child as well as to the local treat-Such care includes instruction in breathing habits, proper ventilation of the bedroom, adjustment of proper bowel function and proper dietary habits. He advises a restriction in sugar intake; candy is forbidden and only a sufficient amount of sugar is permitted to make stewed fruits and cereals palatable. When there is profuse nasal secretion, atropine is given in near physiologic doses. If the child belongs to the vaso-motor group, such furnishings as hair mattresses, feather pillows, carpets and rugs are removed from the sleeping room regardless of the child's response to the skin test. Kapok or cotton mattresses are recommended. Pathologic conditions, regardless of their nature or location, are corrected.

In the local treatment, the author has experienced the best results with the use of glycerine and ichthyol ammonium sulfate applied by means of tamponage at five- to seven-day intervals older children who have had colds for several seasons and who have a dense opacity of the antra, a solution of 20 per cent glycerine and two per cent ichthvol is employed For younger children and for those who have lesser chronicity, a solution of ten per cent glycerine and two per cent ichthyol is all that is required to produce dehydration of the edematous membrane For allergic children with sensitive mucous membranes, a five per cent glycerine and two per cent ichthyol solution is used with a shorter application of three to five minutes This treatment, due to the hydroscopic effect of the glycerine, produces a profuse nasal discharge This dehydration of the water logged nasal mucous membrane and turbinates permits opening of the partially sealed or closed ostium and facilitates emptying of the antrum The author believes this to be a more effective procedure than suction In the older children, the nasal passages are irrigated twice daily by means of the Birmingham douche with a one per cent solution of bicarbonate In younger children, the of soda.

sodium bicarbonate solution may be instilled with a medicine dropper. The author has not observed any instance of primary ear complications from this form of treatment. After four weeks of this treatment, a second roentgenogram of the sinuses is taken. The child is not considered cured until the sinuses are roentgenologically normal and the repeated colds have ceased.

J A Scarano and J F Coppolino³⁴⁰ have experienced good results with the use of benzedrine vapor for the relief of nasal congestion in children preparation is recommended as a substitute for sprays, tampons or "drops in the nose" The benzedrine vapor was administered by means of an inhaler tube (Smith, Kline and French Laborator-Treatment was administered to nursing infants just prior to feeding and to older children when they complained of congestion, but not oftener than once an hour In treating infants, the inhaler was held close to but not touching the nostrils Then by inducing crying, sufficient vapor was inhaled by two inspirations to shrink the nasal mucosa and provide free ventilation Children from three to seven years of age were allowed to hold the inhaler themselves and regulate its proximity to the nostrils The older group, from 7 to 12 years of age, could usually be instructed to insert the tube into the nose, holding one nostril closed, while inhaling twice through the other When this proved difficult, the child was instructed to make a snoring noise which automatically induced inhalation results were obtained in 98 of the 100 cases so treated Results were rated objectively on the amount and duration of shrinkage observed and the relief of congestion, and subjectively by the relief obtained as observed by the parents or reported by the patient Immediate discomfort from the medication was observed in 12 instances. However, in no instance was there any serious untoward reaction

Acute Cervical Adenitis

The use of roentgen rays in the treatment of acute cervical adentis is recommended by S. Hurwitz and S. N. Zuckerman ³⁴¹ Radiation is said to be most beneficial in the early stage of inflammation when absorption is the usual final result. If suppuration is already present before treatment is started, necrosis is hastened and early centralization of infection results. Surgical intervention is minimized and the cosmetic effect greatly enhanced.

Influenza

The recovery of a filtrable virus from children with influenza is reported by I J Brightman and J D Trask³⁴² and by I J Brightman 342a The virus was detected by means of moculation in ferrets as suggested by the work of W Smith, C. H. Andrewes and P. Laidlaw 343 and by that of T. Francis, Jr 344 An agent capable of producing infection of the respiratory tract in feirets was recovered from each of five original specimens of garglings and nasopharyngeal washings of children with symptoms of influenza. No such agent was obtained from the nasopharyngeal washing of one patient with a common cold and from seven patients with measles, although three specimens from the latter group produced an eruption, fever, and leukopenia when inoculated into monkeys. Nor was the infective agent found in the swabbings from the nose and throat of the persons examined during the study of the families of the influenza patients, although five of the members were suffering with infections of the respiratory tract at the time the cultures were made From these experiments it appears that the ferret is susceptible to a filtrable virus found in patients with influenza but is not susceptible by this method of inoculation to the bacteria found in the upper respiratory tract of man. The authors are not willing to state that the demonstration of an infective agent by the method described is a means of differentiating influenza from other diseases, although they believe that such may be the case

Asthma

The inhalation of epinephrine hydrochloride for the relief of asthma in children is recommended by T Graeser and A H Rowe,345 who also describe an apparatus for its administra-The authors state that the relief obtained by this method is comparable and in some respects superior to the relief obtained when this drug is administered hypodermically They have observed no untoward effects from this inhalation of epinephrine in a solution of 1 100 Only with prolonged exposure for periods of from three to four minutes have symptoms such as nervousness, tremor and tachycardia appeared When the inhalations are used as frequently as every hour or less, the only discomfort noticed was an uncomfortable dryness of the mouth and throat This may be minimized when frequent exposure is necessary, by thoroughly rinsing the mouth with water immediately after inhalation

Success with this procedure is dependent upon the use of a stronger solution (1 100) than is usually employed, and the use of an atomizer capable of delivering a fine vapor-like spray. The atomizer employed by the author is shown in Fig. 1. The atomizer has a special feature which prevents spilling of the solution into the mouth

and at the same time delivers a very fine spray. Air pressure for nebulization is furnished by an ordinary rubber bulb. The nozzle of the atomizer is placed just within the open mouth, and the patient inhales deeply while creating a spray. The amount of inhalation varies for each patient and depends not only on the severity of the symptoms but on the manner in which the atomizer is manipulated, such as the vigor with which the

mask apparatus. The nozzle of the atomizer points to the closed end of the mask, so that on pressure of the bulb the mask is filled with vaporized epine-phrine hydrochloride. The mask is placed over the child's face and the child inhales the vapor through the nose and mouth without attempting to co-ordinate with compression of the bulb From 30 to 45 seconds exposure is usually sufficient.

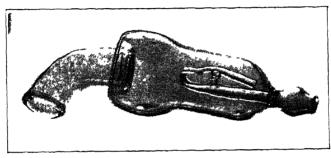


Fig 1—An atomizer with the nonspill feature (Courtesy, Amer J Diseases of Children, July, 1936)

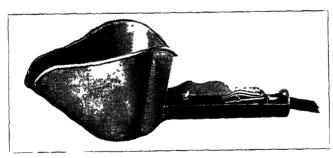


Fig 2-Mask and atomizer (Courtesy, Amer J Diseases of Children July, 1936)

bulb is compressed and the correlation of inhalation with compression of the bulb. The patient is advised to proceed slowly, allowing one or two minutes to elapse between several deep inhalations, until he has determined the amount necessary for the relief of symptoms. For the use of children from one to two years of age, the authors have devised a mask (Fig. 2) which is designed to conform with the configuration of the face and to cover the nose and mouth. An atomizer fits into the handle of the

Pneumonia

A study of *pneumonia* in infants and children based upon the type of infecting pneumococcus has been conducted by J G M Bullowa and E Greenbaum ³⁴⁶ TABLE I taken from their article, shows the mortality in their series of 539 cases according to the type of pneumococcus and the age of the patient. Their data indicate that certain types of pneumococci affect children of certain ages. The important types are I, VI, XIV and XIX. Types VI and XIV attack

TABLE 1

MORTALITY ACCORDING TO THE TYPE OF PNEUMOCOCCUS AND THE AGE OF THE PATIENT

| | | Total | | Pa | atient U 2 Year | | | atient F to 12 Y | |
|--|---|--|---|---|--|---|--|---|--|
| Type of Pneumococcus | No of Cases | No of Deaths | Per- centage | No of Cases | No of Deaths | Per- centage | No of Cases | No of Deaths | Per- centage |
| I II III IV V VI VII VIII IX X XI XII XI | 79 11 25 30 29 55 17 12 7 6 3 0 4 83 4 7 3 9 25 3 9 4 9 5 0 | 6 1 4 4 3 11 2 2 2 1 0 0 2 12 2 2 1 0 0 0 0 0 0 0 | 7 6 9 1 16 0 13 3 10 3 20 0 11 8 16 7 28 6 16 7 0 0 50 0 14 5 50 0 28 6 33 3 0 0 12 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 | 13 5 9 13 7 34 5 6 4 6 0 0 4 47 3 4 3 4 19 2 6 2 7 1 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 | 3 1 2 4 3 8 1 2 1 1 0 0 2 7 2 1 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 | 23 1 20 0 22 2 30 8 42 9 23 5 20 0 33 3 25 0 16 7 0 0 0 0 14 9 66 7 25 0 33 3 0 0 15 8 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 | 66 6 16 17 22 21 12 6 3 0 3 0 0 3 6 1 3 0 5 6 1 3 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 | 3 0 2 0 0 0 3 1 0 1 0 0 0 0 5 0 1 0 0 0 0 0 1 0 0 | 45 00 125 00 00 143 83 00 00 00 00 00 00 00 00 00 00 00 00 00 |
| XXVII XXVIII XXIX XXXX XXXI XXXII "\"\" Multiple infections | 1 1 8 4 1 0 70 15 | 0 1 1 0 0 0 0 12 7 | 0 0 100 0 12 5 0 0 0 0 0 0 17 1 46 7 | 1 1 7 3 0 0 0 39 7 | 0 1 1 0 0 0 0 11 5 | 0 0 100 0 14 3 0 0 0 0 0 0 28 2 71 4 | 0 0 1 1 1 0 31 8 | 0 0 0 0 0 0 1 2 | 0 0 0 0 0 0 0 0 0 0 0 0 3 2 25 0 |
| Total | 539 | 83 | 15 4 | 262 | 63 | 24 0 | 277 | 20 | 7 2 |

^{*} Type XXVI or VIb, is included with type VIa as type VI (Courtesy, American Journal of Diseases of Children, January, 1937)

principally children under six years of age, type I, children over six years and in this series types VIII and XIX attacked only children under six, whereas type III, IV, V, VI and VII attack children of all ages Types II, IX and XVIII which frequently affect adults are uncommonly seen in children Unclassified strains of pneumococci are found more frequently in children than in adults The mortality in this series for primary lobar pneumonia due to

pneumococci was less than half that for primary bronchopneumonia due to pneumococci

A R Macgregor³⁴⁷ reports ten instances of *staphylococcic pneumonia* in infants and small children. She believes that her pathologic data reveal sufficiently constant and distinctive features to designate primary staphylococcic pneumonia as a clinical and pathologic entity. In each instance there was unilateral empyema and in three a pyo-

pneumothorax A localized area of suppuration was invariably present in the corresponding lung This area varied in size but was often quite small Within the affected region there were multiple ramifying abscesses, one or more of which had burst through the pleura. Typically there was an absence of generalized bronchitis and of consolidation in either lung apart from the single area of suppuration In nine instances staphylococcus aureus was 150lated and in one staphylococcus albus In six instances the staphylococcus was the only infecting micro-organism isolated The intimate relation of many of the abscesses to bronchi, and the severe purulent inflammation of the bronchial walls, even in the earlier stages, together with the absence of septic thrombi of the pulmonary arteries, are features which the author believes practically prove that the route of invasion is bronchial and not vascular

Roentgenologic evidence that so-called central or hilar pneumonic lesions may actually extend towards the periphery of the lung has been presented by A Carrau and H C Bazzano 348 In those instances in which anterioposterior roentgenograms of the chest revealed a central pneumonic shadow, the authors made lateral and oblique roentgenograms. In all of their cases they were able to demonstrate that the lesion extends towards the periphery either in the middle or in one of the lower lobes. The clinical course was characteristic of pneumonia.

A face mask for oxygen administration for newly born infants is described by H A Agerty and C M Witzberger 349 The apparatus consists of a large rubber nipple, of the type employed for wide neck nursing bottles The tip of the nipple is cut off and a glass connecting tube is inserted into it. The

other end of the glass tube is attached to a rubber tube coming from the oxygen supply. The large opening of the nipple fits rather closely over the infant's face, covering both the nose and mouth. This face mask is attached to the infant's head by a simple harness made of adhesive tape and gauze bandage. While the approximation of the mask to the face is close, there is enough free space to allow for the escape of exhaled air. The rate of oxygen flow may be regulated according to the clinical needs of the patient

Bronchiectasis

Assuming that mechanical obstruction is one of the most important factors in the production of bronchiectasis, G B Ferguson³⁵⁰ believes that in many instances bronchiectasis could actually be prevented if the obstruction is removed sufficiently early. In those instances when bronchiectasis originates during or shortly after the acute infectious diseases of childhood, the author believes that it might have been prevented if bronchoscopic aspiration had been employed during the acute stage, thus aiding aeration and drainage of the lung is suggested that bronchoscopic examination be performed on those children who have a chronic cough or who have repeated pulmonary infections and in whom pulmonary tuberculosis has been ruled out

While there is no doubt that the bronchoscope has and is providing new methods of diagnosis and treatment, the fact should be emphasized that its use should be limited to those who are not only thoroughly trained but entirely competent. Otherwise it is apt to be unfairly discredited and its further use delayed.

Lung Abscess

According to F P Mathews³⁵¹ non-tuberculous pulmonary abscesses are not

only being diagnosed more frequently in children in recent years but there seems to be an actual increase in their incidence This, he suggests, may be due, among other things, to the high rate of tonsillectomies The author has studied 12 cases of nontuberculous lung abscesses in children under ten years of age In comparison with lung abscesses in adults, the prognosis seems to be more Aspiration seems to be the favorable most common route of invasion clinical courses of the author's cases varied considerably. In those instances when the cause of the abscess was known definitely to be due to aspiration, an incubation of from 10 to 14 days was noted The course of the disease could be roughly divided into three stages invasion, cavitation and emptying of the The onset was that of an acute infection with sudden appearance of high fever, chills, tachycardia, chest pains, cough and a leukocytosis of about 25,-Various physical findings were noted in the chests of these children and the author states that, while general location of the lesions and the progress of cavitation can be judged by the stethoscope much more accurate information may be had from the roentgenogram The abscess may rupture and drain into a main bronchus or into the pleura Unless such an accident occurs it is stated that in general a level is reached in about three weeks, at which time the condition tends to become chronic

During the acute stage the author recommends that the child should be treated essentially as if it had lobal pneumonia. If pus from the abscess is available, it should be examined bacteriologically, and if a fusospirochetal or a fungus infection is discovered, it may be treated with *arsphenamine* or *iodides*. Tuberculosis should be ruled out by means of

a tuberculin test, the roentgenogram and the examination of the sputum for tubercle bacilli As soon as the condition of the child permits, daily postural drainage should be instituted. If, after approximately six weeks of medical treatment, adequate drainage has not resulted, an attempt should be made to drain the abscess, either through the bronchoscope, especially when the abscess is situated near the root of the lung or in one of the lower lobes, or by thoracotomy, if it is located near the periphery of the lung For external drainage, the author prefers the two-stage thoracotomy. In the first stage, about one and one-half inches of rib is resected, as nearly as possible over the abscess as indicated by the roentgenogram The rib bed is packed with 10doform gauze in order to induce adhesions about the operative wound to prevent a pneumothorax About five days after the first stage operation, adhesions have formed sufficiently to permit the exploration of the lung periphery at the site of the first stage operative wound Exploration is made with a needle and when pus is found, an incision is made along the needle as a guide. The author recommends the use of the electro-cutting knife in order to minimize bleeding. The cavity is then packed and treated subsequently as an ordinary empyema

Pulmonary Gangrene

According to J W Epstein, ³⁵² pulmonary gangrene occurs more frequently in children than reports in medical literature would indicate. It is suggested that this is due in part to a confusion of pulmonary gangrene with pulmonary abscess. He points out that pulmonary gangrene is a distinct clinical entity and should not be confused with pulmonary abscess. Abscesses are produced by pyogenic organisms which never produce

gangrene, whereas gangrene results from invasion of pulmonary tissue by spirochete, fusiform bacilli and vibrios (Miller-Vincent Organisms) The differentiation of pulmonary gangrene from pulmonary abscess, in view of their clinical, anatomic and roentgenologic resemblance, 15 to a large extent dependent upon a study of the character and bacteria of the sputum The sputum from abscesses is mucopurulent or purulent, has no appreciable odor and the washed specimen contains pyogenic organisms. In contrast, the sputum from a gangrenous lesion is foul smelling, greyish brown or greyish green and when washed reveals spirochetes, fusiform bacilli and vibrios The penetratingly foul odor emanating when the patient coughs is one of the characteristic clinical symptoms and is suggestive of pulmonary gangrene The presence in children of an associated oral lesion, usually dental caries or gingivitis, containing large numbers of oral spirochetes, is suggestive of the character of a pulmonary lesion when sputum is not obtainable This finding is particularly significant in children below the age of ten years, since their oral flora seldom include the Miller-Vincent organisms

The medical treatment of pulmonary gangrene includes general care, postural drainage, arsenical therapy and prophylaxis In the author's experience, the intravenous administration of arsenic in the form of neoarsphenamine is the most valuable single measure (See also under Diseases of the Digestive System in Children) The arsphenamine is administered in doses of 0.01 gram per kilogram of body weight every third day until the sputum has lost its odor and the physical findings have disappeared Should toxic symptoms appear, such as itching of the skin, jaundice, gastroenteric upset or renal involvement, further arsenical treatment should be discontinued immediately. Since five of the author's cases occurred after tonsillectomy and since in all five instances smears of material taken from the interproximal spaces between the teeth and gums showed Miller-Vincent organisms, the author suggests, as a matter of prophylaxis, that tonsillectomy should not be performed in the presence of oral infection with fusospirochetal organisms. The operation should be delayed until this infection is removed

Pleurodynia

Clinical and bacteriologic studies have been carried out during an epidemic of pleurodyma or epidemic myalgia by R R Macdonald. B Hewell and M L Cooper 353 As it usually does, the epidemic occurred during the summer months and at the same time as an epidemic of benign lymphocytic meningitis 354 The question was raised whether the causative agent of these two diseases might be identical, in one instance the central nervous system being affected and in the other the peripheral nervous system The diagnosis of the disease rests primarily on the acute onset with pain and fever the absence of physical signs to account for the symptoms, the tendency to recurrence of fever and symptoms and the quick recovery without sequellae Diagnosis is difficult except in the presence of an epidemic The disease in children is most frequently confused with acute appendicitis, early pneumonia or pleurisy and in adults with acute cholecystitis, influenza or coronary occlusion Differentiation is based on the colicky, knife-like character of the pain, the absence usually of localized tenderness in the right lower part of the abdomen, the absence of involuntary spasm of the muscles in most instances and the relatively low leukocyte count Bacteriologic studies have not revealed the causative agent

SCARLET FEVER

By ROBERT A LYON, AB, A.M, MD

The behavior of the erythrocytic sedimentation test in patients with scarlet fever and its complications has been reviewed recently by J. S Cookson 355 A series of 76 patients, ranging in age from 3 to 30 years, was selected for examination and the tests were performed on the fourth, fourteenth and twenty-fourth days of the disease in the majority of instances In uncomplicated cases, the first sedimentation rate was relatively high but the subsequent ones gradually receded during the next three weeks Normal figures were not generally reached even by the twenty-fourth day Complications such as nephritis, otitis media and cervical adenitis caused a subsequent elevation of the sedimentation rate or resulted in a sustained high rate which did not recede as in normal patients. There was a tendency for the rate to rise before the clinical evidence of the complication became apparent in some patients and it fell after successful treatment of the condition The test was found to be of value in differentiating albuminuria of benign types from that of true nephritis Serum reactions caused no rise in the sedimentation rate. It was the conclusion of the author that serial sedimentation tests in scarlet fever patients would generally indicate the development of complications and the efficacy of treatment

Variations in the serological types of hemolytic streptococci were found in an epidemic of scarlet fever in Edinburgh observed by C. A. Green 356. By the use of agglutination reactions he was able to demonstrate the presence of at least eight different serologic types of hemolytic streptococci in a single epidemic. The prevalent type of streptococcus varied from month to month during the epidemic, in spite of the fact that the age

groups affected by the disease were much the same as in previous years Previous investigations had shown that there was little variation in the type of toxin produced by these different strains of bacteria. About five per cent of the group of patients who were examined at the time of their discharge from the hospital had sufficiently large numbers of streptococci in their throats to be of danger as carriers of the disease. In the great majority of instances the strains of bacteria found at the time of discharge were identical to those which had been isolated from the patient at the time of his admission to the hospital

Complications—The possibility that many of the complications and relapses occurring in scarlet fever patients, especially of those who are treated on open wards, may be the result of reinfection. has been suggested by the work of V D Allison and W A Brown 357 Bacteriologic examinations were made of a group of patients when they were admitted to the hospital with scarlet fever and all were found to harbor strains of streptococci which were serologically of the scarlet fever types In a group of 47 patients who were cared for on an open ward, 70 per cent subsequently became infected with a streptococcus of a different strain, usually at a time about three weeks after the onset of their original illness Fifteen of the group of 33 patients who developed other strains of streptococci in their nose and throat secretions, remained free from illness, but the remainder of the group developed complications Patients who developed a relapse of the scarlet fever were all of the groups which had been cared for on open wards Patients who had been treated in cubicles or in separate rooms rarely developed secondary infections or relapses It was the opinion of the author that many of the infections and complications of scarlet fever are the result of cross infection spread by direct contact with other patients. The treatment and prevention of this condition seemed to be the isolation of every scarlet fever patient so that he would avoid contracting a streptococcus infection of another type The shortening of the isolation period has been found by some clinicians to be a method for reducing the incidence of complications but the author believed that this was not sufficient precaution and that patients must also be isolated from each other during their hospital stay

Encephalitis following many of the contagious diseases has received considerable attention in the past few years The occurrence of this complication in a patient with scarlet fever is rare Such a case was observed recently by R Martin and P Champion 358 A boy, six years of age, developed symptoms of headache on the twenty-fourth day after the onset of a mild attack of scarlet fever. Fever. vomiting, somnolence, signs of meningeal irritation, and finally, coma and convulsions developed in rapid succession. In the cerebrospinal fluid, which was under increased pressure, were 35 cells and an elevation of the albumin content Within four days the symptoms subsided and during the next two weeks the child made a complete recovery In a review of 22 previous reports of this type of complication in scarlet fever, occurring in the medical literature of the last 48 years, the authors noted that eight cases had occurred in patients six to ten years of age, 11 in patients 11 to 20 years old and three in those who were over 21 years of age The disease developed at various stages of the scarlet fever, from the time of the appearance of the eruption to the fiftieth day after the onset The symptoms of most of the reported cases resembled those described above, although there were variations in some instances in the portion of the nervous system which was primarily involved Evidence of cerebellar lesions was occasionally seen while other forms were of the hemiplegic type or included paralysis of the peripheral nerves The cerebrospinal fluids usually contained increased numbers of cells, mostly lymphocytes, slight elevations of protein content but no abnormalities of sugar content and no bacteria The outcome of the disease was not always favorable and some reports listed such residual damage as amyotrophy, paresis and psychic dis-Pathological studies came turbances from only one source and included the finding of ventricular hemorrhage, thrombosis of numerous cerebral vessels, edema of the brain and superficial areas of The etiology is still undeternecrosis mined

Streptococcic peritonitis is one of the less common complications of scarlet In the patient observed by D Erskine, 359 the symptoms began on the twenty-second day after the onset of scarlet fever and immediate operation was undertaken The thin pus recovered from the abdomen contained hemolytic streptococci The patient died 10 hours later and at autopsy there was found an enlarged mesenteric gland which had suppurated and discharged a thick green pus From the few cases of peritonitis following scarlet fever which have been reported previously in the medical literature, it seemed that the complication could appear early in the course of the disease as the result of septicemia, or later as a result from inflammation of mesenteric glands The author suggested that mesenteric adenitis might be a more

common lesion in scarlet fever than has been previously recognized clinically

Treatment - Antitoxin treatment of patients with scarlet fever relieves the symptoms and reduces the incidence of complications With such therapy, the period of isolation has been shortened This subject has been reviewed lately by H S Banks 360 The results from treating 1877 patients with 10 to 20 cc of antitoxin administered intravenously were compared with those of 1419 untreated patients on other wards treated patients usually felt free of pain m 12 hours, the rash faded by 24 to 36 hours, they are normal diets by the third day and were allowed up on the fifth to seventh day Children were discharged 14 to 21 days after the onset of the illness and adults were allowed to go home on the tenth to fourteenth day Although the opportunity to observe such patients closely for complications was less than if they had remained in the hospital longer. the reports from other physicians and from the patients themselves indicated that they had remained free from untoward after-effects of the disease As a rule, the number of complications in the treated groups were less than half as great as in the control series, but the incidence of otitis media was reduced to one-third and that of nephritis to oneseventh of the incidence in the control series ()nly two of the treated patients died as compared to 12 of the untreated group These figures were further enhanced by the fact that there was a tendency to administer serum to the most severe cases

In comparing the *intravenous route* with the *intraperitoneal method* of administration of serum to alternate patients in a group of about 1000 patients, the authors found the results to be equally good. The dosage of antitoxin was 10 to 20 cc., depending upon the age of the

patient and the severity of the initial symptoms of the disease. The results were most satisfactory when the serum was administered early in the course of the infection, preferably during the first three days of illness Reactions varied with various commercial brands of scarlet fever antitoxin and were often quite severe when the intravenous method of administration was employed The intraperitoneal route of administration caused abdominal pain, tenderness and rigidity in 75 per cent of instances with one brand of antitoxin but generally the symptoms were very mild and systemic reactions rare, comparing favorably in this respect with the intramuscular methods of administration but probably giving a quicker therapeutic response because of the increased rapidity of absorption

Immunization—Immunization by intracutaneous injections of antigen has been employed in several diseases and recently the method has been applied to scarlet fever by J H Robinson 361 Twenty-four patients of an average age of 21 years, ranging from 2 to 39 years old, who had not had scarlet fever and were Dick positive, received 7000 to 10,000 units of scarlet fever toxin intradermally in five or six successive injec-The toxin was administered at five-day intervals, beginning with 50 units as the initial dose and ending with 3600 to 7200 skin test doses. All patients became Dick negative when tested two weeks after the termination of the treatment but the duration of the immunity has not vet been determined. The technic of the intracutaneous injection was the same as that employed for the Dick test ıtself

About three per cent of the number of young adults who receive active immunization against *scarlet fever* develop joint pains as a complication of the therapy In order to determine whether it was the

scarlet fever toxin or the other protein material present in the medication which was responsible for this disease, C E Healev362 conducted a series of experiments on 63 young adults. All of these patients had complained of joint pains following the administration of the first immunizing dose of scarlet fever toxin The author then gave alternate injections of regular toxin and similar material which had been heated for one hour to remove the toxic products About 75 per cent of the group developed joint pains following the injection of toxin only, about 17 per cent developed severe joint pains following the injection of the toxin and less severe pain following the injection of the heated toxin About eight per cent developed joint pains regardless of the material which was injected Of the entire group at least 84 per cent had had a history of previous rheumatic or joint infection. It was the conclusion of the author that the joint pains which occurred after the injection of scarlet fever toxin generally resulted from the toxin itself and not from the other protems of the veal broth culture in which the toxin had been prepared. It was an interesting observation that many patients who had previous rheumatic joint infections developed local reactions when a toxin of another nature was injected into their bodies

The Dick Test—The Dick test for testing an individual's susceptibility to scarlet fever has never proved as accurate as the Schick test for diphtheria. The occurrence of negative Dick tests early in scarlet fever, the presence of positive reactions during convalescence from that disease and the occurrence of scarlet fever in Dick negative patients has led F L Ker³⁶³ to conduct further experiments in the determination of factors which may lead to the inaccuracy of the test. The technic of performing

the tests is difficult because it requires the injection of an exact amount of toxin into the skin, and the reading of the test is difficult because of the faint and the transient nature of the reactions which must be observed from 12 to 18 hours after the test is performed lighting, close observation and experience are necessary for the proper interpretation of the reaction The scarlet fever toxin is relatively instable with heat but it is necessary to expose the toxin to temperatures of boiling for at least four hours to completely mactivate The toxin likewise deteriorates with storage but it was found that it could be kept for a period of six weeks without reducing its potency, especially when a stabilizing mixture was added to it The effect of dilution upon a toxin did not always reduce the size of a patient's skin reaction so that when one sample of toxin was compared with another, standardization could not be determined unless a group of at least 50 susceptible patients were used in the comparative tests. In the author's experience pseudoreactors were rare, although occasionally a patient would show a reaction to a heated toxin product which contained no active toxic elements

Many of the discrepancies in the Dick test have been attributed by S Thomson364 to the variations in methods of preparation and of standardization of the scarlet fever toxin. By the use of skin reactions and neutralization tests he has found considerable similarity between the exotoxin of the streptococcus of scarlet fever, puerperal fever and erysipelas The antitoxin prepared from the toxin injected into animals neutralized all of this group of toxins In order to obtain more accurate results from the testing of immunity to scarlet fever with the Dick reaction it was suggested that a more potent toxin containing 100,000

skin test doses per cc be employed Another procedure which is important in obtaining a true response to the toxin is the use of a filtrate which has been obtained from a culture of bacteria which is not more than 24 hours old. It seemed that the more prolonged growth of the bacteria soon resulted in autolysis which produced proteins which gave positive skin reactions but did not represent the true response of a patient to the toxin

itself Endotoxins, which are prepared from the bacterial bodies of the streptococcus, tended to give the same type of skin reaction regardless of whether the source of the hemolytic streptococcus was from scarlet fever, puerperal fever or erysipelas infections. Many of the discrepancies in the Dick reaction may be due to the presence of autolytic endotoxin in the test material instead of the pure exotoxin filtrate.

CONGENITAL SYPHILIS

By Robert A. Lyon, A.B., A.M., M.D.

The discovery of syphilis in the newborn is difficult because of inaccuracies of the serological tests at that age The need for more adequate criteria for the diagnosis of the disease has been urged by F W Cregor and J E Dalton 365 The 65 syphilitic mothers under their observation represented two per cent of their clientele About 92 per cent of this group had received some antiluetic treat-More than three-fourths of the patients had either inactive or congenital types of syphilis The serologic tests of the cord blood of the newly-born infants were positive with the Wassermann technic in about half of the number and in only 15 per cent with the Kahn reaction Blood obtained from the jugular veins of the newborn were positive in 24 per cent by the Wassermann test and in only nine per cent by the Kahn or Kline tests. The authors believed that the positive serologic test in the newborn indicated a syphilotoxemia only and that reversals frequently took place within the first 14 days of life

The clinical manifestations of syphilis and the results of treatment of more than 1000 children have been reviewed recently by members of the Co-operative

Clinical Group and the United States Public Health Service The patients had attended clinics of the Universities of Western Reserve, Johns Hopkins, Pennsylvania, Michigan and the Mayo Clinic, and the summary and conclusions were reported by H N Cole L J Usilton, J E Moore, P A O'Leary, J H Stokes, U J Wile, T Parran, Jr, and R A Vonderlehr 366 The group of children numbered 1010, all more than two vears of age on admission to the clinic and they had been under observation for a period of at least two years White patients of the group numbered 705 and the negroes, 305 Acute lesions, of less than six months duration, were noted in 22 per cent of the group, chronic lesions or those which had existed for more than six months, occurred in 28 per cent, inactive scars such as saddle nose deformities, corneal opacities, were present in 11 per cent, and latent syphilis with no visible lesions in 39 per cent The incidence of latent syphilis was twice as great in the negro race as in the white, indicating that the disease affected the white children more severely than the colored The incidence of various lesions is indicated by the accompanying table

TABLE 1

PRINCIPAL DIAGNOSIS AND FREQUENCY OF EACH MANIFESTATION ON ADMISSION OF PATIENTS WITH LATE PRENATAL SYPHILIS

| Principal Diagnosis on Admission | White | | Ne | gro | Total | Cases | Frequency of Each Manifestaion | |
|--|----------------------|--------------------------|------------------|--------------------------|----------------------|--------------------------|--------------------------------------|--------------------------|
| | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age |
| Latent syphilis | 214 | 30 4 | 183 | 60 0 | 397 | 39 3 | 397 | 39 3 |
| Involvement of the skin and mucous membrane Involvement of the bones and joints Interstitial keratitis Involvement of the eye (other than | 28 50 258 | 4 0 7 1 36 6 | 9 18 71 | 3 0 5 9 23 3 | 37 68 329 | 3 7 6 7 32 6 | 57 115 403 | 5 6 11.4 39 9 |
| interstitial keratitis or atrophy of the optic nerve) Atrophy of the optic nerve Nerve deafness Visceral involvement Involvement of the central nervous | 13 10 26 12 | 1 8 1 4 3 7 1 7 | 2 1 6 5 | 0 7 0 3 1 9 1 6 | 15 11 32 17 | 1 5 1 1 3 2 1 7 | 39 25 59 37 | 3 9 2 5 5 8 3 7 |
| system Asymptomatic | 24 | 3 4 | 4 | 1 3 | 28 | 28 | 57 | 5 6 |
| Symptomatic Meningovascular disease Dementia paralytica Tabes dorsalis | 13 41 16 | 1 8 5 8 2 3 | 3 3 | 1 0 1 0 | 16 44 16 | 1 5 4 4 1 5 | 19 46 18 | 1 9 4 6 1 8 |
| Total | 705 | 100 0 | 305 | 100 0 | 1,010 | 100 0 | 1,272 | 125 9 |

(Courtesy, Arch Dermat and Syph, April, 1937)

TABLE 2

Results of Treatment in Terms of Clinical Outcome in Patients with Late Prenatal Syphilis

| Stage of Late Prenatal Syphilis When Treatment Was Begun | Clinical Outcome | | | | | | | | | | | |
|---|------------------------|------------------------------|-----------------------|-----------------------------|------------------------|----------------------------|-------------|----------------------|--------------------------|--------------------------|--|--|
| | Satis- factory | | Not Satis- factory | | Progress or Relapse | | Death | | Total | | | |
| | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age | | |
| Acute lesions Chronic lesions Inactive stage with residual scars Latent syphilis | 129 84 26 377 | 57 3 30 2 23 7 95 0 | 74 130 70 6 | 32 9 46 8 63 6 1 5 | 21 52 14 14 | 9 3 18 7 12 7 3 5 | 1 12 | 0 5 4 3 | 225 278 110 397 | 100 100 100 100 | | |
| Total | 616 | 61 0 | 280 | 27 7 | 101 | 10 0 | 13 | 1 3 | 1,010 | 100 | | |

(Courtesy, Arch Dermat and Syph, April, 1937)

TABLE 3

Effect of Fined Serologic Reaction of the Blood on Clinical Outcome in Patients with Late Prenatal Syphilis in Each Stage of the Infection

| | Clinical Outcome | | | | | | | | | | | |
|---|-------------------|----------------------|-----------------------|----------------------|------------------------|----------------------|-------------|----------------------|-------------|----------------------|--|--|
| Stage of Late Prenatal Syphilis When Treatment Was Begun | Satis- factory | | Not Satis- factory | | Progress or Relapse | | Death | | Tot | al | | |
| | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age | | |
| Acute lesions Serologic reaction of the blood Fixed Not fixed Chronic lesions | 60 69 | 51 3 63 9 | 42 32 | 35 9 29 6 | 14 | 11 9 6 5 | 1 | 09 | 117 108 | 100 100 | | |
| Serologic reaction of the blood Fixed Not fixed Inactive stage or residual scars | 45 39 | 27 8 33 6 | 75 55 | 46 3 47 4 | 31 21 | 19 1 18 1 | 11 1 | 6 8 0 9 | 162 116 | 100 100 | | |
| only Serologic reaction of the blood Fixed Not fixed Latent syphilis | 8 18 | 15 4 31 0 | 36 34 | 69 2 58 6 | 8 6 | 15 4 10 4 | | | 52 58 | 100 100 | | |
| Serologic reaction of the blood Fixed Not fixed Total | 203 174 | 94 8 95 1 | 1 5 | 0 5 2 7 | 10 4 | 4 7 2 2 | | | 214 183 | 100 100 | | |
| Serologic reaction of the blood Fixed Not fixed | 316 300 | 57 9 64 5 | 154 126 | 28 3 27 1 | 63 38 | 11 6 8 2 | 12 | 2 2 0 2 | 545 465 | 100 100 | | |
| Grand total | 616 | 61 0 | 280 | 27 7 | 101 | 10 0 | 13 | 1 3 | 1,010 | 100 | | |

(Courtesv Arch Dermat and Syph, April, 1937)

The treatment of the early active lesions gave satisfactory results in 57 per cent of instances. The result was considered satisfactory if the lesions disappeared, regardless of any change in the serologic tests. An additional 33 per cent of the children showed good results from treatment but scars of the infection remained. When treatment was instituted later in the course of the active lesion, the percentage of satisfactory results dropped to 24 and 30, while treatment instituted before active lesions occurred led to good results in 97 per cent of instances. (See Table 2.)

The response of the blood serologic reaction to treatment did not seem to be related to the amount of therapy given Half of the group had fixed serologic reactions regardless of treatment Most of the children who had reversals of then serologic tests developed negative reactions by the end of one year of treat-Patients with active lesions or residual scars, who had serologic reversals, progressed better than the average of the other patients Children with latent syphilis, who had never had visible lesions of the disease, seemed to make as good clinical progress under treatment as did those whose tests remained fixed when their serologic reactions became negative The figures indicated that early and continuous treatment of a patient for more than a year was highly effective in clearing up the clinical manifestations

TABLE 4

Effect of Prolonged Treatment and Fixed Serologic Reaction of the Blood on the Clinical Outcome in Patients with Late Prenatal Syphilis, Stage of the Infection When Treatment Was Begun

| | Clinical Outcome | | | | | | | | | | | |
|---|-------------------|----------------------|-----------------------|----------------------|------------------------|----------------------|-------------|----------------------|-------------|---|--|--|
| Stage of Late Prenatal Syphilis When | Satis- factory | | Not Satis- factory | | Progress or Relapse | | Death | | Total | | | |
| Treatment Was Begun | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age | | |
| | Less | Than | One Y | ear | | | | | | e de la composição de la c | | |
| Latent syphilis Serologic reaction of the blood Fixed Not fixed | 22 9 | 95 7 100 0 | 1 | 43 | | | | | 23 9 | 100 | | |
| Total | 31 | 96 9 | 1 | 3 1 | | | | | 32 | 100 | | |
| Active or inactive stage Serologic reaction of the blood Fixed Not fixed | 2 5 | 7 4 26 3 | 13 | 48 2 57 9 | 9 3 | 33 3 15 8 | 3 | 11 1 | 27 19 | 100 | | |
| Total | 7 | 15 2 | 24 | 52 2 | 12 | 26 1 | 3 | 6 5 | 46 | 100 | | |
| Total (less than one year) | 38 | 48 7 | 25 | 32 1 | 12 | 15 4 | 3 | 3 8 | 78 | 100 | | |
| | On | e Year | or Mo | ore | | | | | | Ţ | | |
| Latent syphilis Serologic reaction of the blood Fixed Not fixed | 181 165 | 94 8 94 8 | | 29 | 10 4 | 5 2 2 3 | | | 191 174 | 100 | | |
| Total | 346 | 94 8 | 5 | 1 4 | 14 | 3 8 | | | 365 | 10 | | |
| Active or inactive stage Serologic reaction of the blood Fixed Not fixed | 111 | 36 5 46 0 | | 46 0 41 8 | | | | | | 10 | | |
| Total | 232 | 40 9 | 250 | 44 1 | 75 | 13 2 | 10 | 18 | 567 | 10 | | |
| Total (more than one year) | 578 | 62 (| 255 | 27 4 | 89 | 9 5 | 10 | 1 1 | 932 | 10 | | |

TABLE 5

CLINICAL RESULTS IN LATE PRENATAL SYPHILIS, THE DURATION OF THE PERIOD OF OBSERVATION AFTER THE TERMINATION OF TREATMENT

| | | Clinical Outcome | | | | | | | | | | | |
|---|-----------------------|-------------------------------|----------------------|------------------------------|--------------------|------------------------------|------------------------|----------------------------|--|--|--|--|--|
| Duration of Period of Observation | Satisfa | Satisfactory | | Not Satisfactory | | ress lapse | Total | | | | | | |
| | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age | | | | | |
| | ! | P | atients | with La | tent Syp | hilis | | | | | | | |
| Less than 2 years 2–5 years 6–10 years 11 years and over | 269 71 25 10 | 94 4 97 2 96 2 100 0 | 4 1 | 1 4 1 4 | 12 1 1 | 4 2 1 4 3 8 | 285 73 26 10 | 72 3 18 5 6 6 2 6 | | | | | |
| Total | 375 | 95 2 | 5 | 1 3 | 14 | 3 5 | 394* | 100 0 | | | | | |
| | 1 | Patie | nts with | Active | Lesions | or Scar | 'S | | | | | | |
| Less than 2 years 2-5 years 6-10 years 11 years and over | 146 58 25 4 | 37 3 40 8 42 4 40 0 | 191 62 25 5 | 48 7 43 7 42 4 50 0 | 55 22 9 1 | 14 0 15 5 15 2 10 0 | 392 142 59 10 | 65 0 23 5 9 8 1 7 | | | | | |
| Total | 233 | 38 7 | 283 | 46 9 | 87 | 14 4 | 603* | 100 0 | | | | | |

^{*}The total does not include 13 patients in whom syphilis was given as the cause of death (Courtesy, Arch Dermat and Syph, April, 1937)

of syphilis The lapse of time before symptoms of syphilis developed did not insure the children against progression of the disease. In spite of treatment, 14 per cent of those with active lesions had further progression of active syphilis, while only four per cent of those receiving treatment before active lesions developed, showed progressive lesions in later years. (See Tables 3, 4 and 5.)

Especial attention was given in the survey to the problem of *interstitial keratitis* which was the most frequent symptom of late congenital syphilis. It was the lesion which led 36 per cent of the group to seek medical care. Untreated, the condition may occur throughout the age period of 5 to 25 years. Treatment of congenital syphilis in the early years of a patient's life tends to reduce the occur-

rence of keratitis as was shown by the finding that only two per cent of syphilitic children who had received adequate antiluetic treatment before symptoms occurred, developed the eye lesions Even inadequate treatment reduced the incidence from 36 to 9 per cent When keratitis developed in one eye, adequate treatment begun within the next six months was found to prevent the occurrence of the condition in the other eye, but without adequate therapy the second eye was involved in 87 per cent of instances within a period of the next two years If this event can be prevented by treatment for that period of time, the chances of the lesion occurring in the second eye were thought to be slight

The essential factors in the treatment of the interstitial keratitis were early

TABLE 6

Effectiveness of Treatment for Late Prenatal Syphilis in Preventing
Interstitial Keratitis

| Amount of Treatment Received* | | Number of Patients Exhibiting | Total Number | Percentage Exhibiting Interstitial | | |
|----------------------------------|--------------|-------------------------------------|--------------|--|--|--|
| Arsenical | Interstitial | | Patients† | Keratitis | | |
| No. | one | 314 | 884 | 35 5 | | |
| Heavy m | etal alone | 10 | 18 | 55 6 | | |
| Little | Little | 13 | 150 | 8 7 | | |
| Little | Much | 4 | 43 | 93 | | |
| Much | Little | 4 | 130 | 31 | | |
| Much | Much | 5 | 243 | 2 1 | | |
| wucn | Iviuch | 3 | 243 | | | |

^{*}Little arsenical means from 1 to 15 injections, much arsenical means 16 or more injections Little heavy metal means from 1 to 30 injections or weeks of mercury rubs, much heavy metal means 30 or more injections or weeks of mercury rubs

TABLE 7

CLINICAL RESULTS FROM MODERN ANTISYPHILITIC TREATMENT BEGUN IN THE VARIOUS STAGES OF INTERSTITIAL KERATITIS

| | Stage of Interstitial Keratitis at Which Treatment Was Begun | | | | | | | | | | | |
|---|--|---------------------------------|------------------------|----------------------------------|--------------|----------------------------------|-----------------------------|---|--------------------------------|---|--|--|
| Clinical Results of Treatment | Early Acute* | | Late Acute | | Relapsing | | Inactive | | Total | | | |
| | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age | Num- ber | Per- cent- age | | |
| Satisfactory Excellent Good Arrest | 55 22 52 | 35 0 14 0 33 1 | 25 4 38 | 28 7 4 6 43 7 | 6 11 23 | 10 9 20 0 41 8 | 10 15 34 27 | 7 8 11 6 26 4 20 9 | 100 54 34 125 | 23 4 12 6 7 9 29 2 | | |
| Improvement Total | 129 | 82 2 | 67 | 77 0 | 40 | 72 7 | 86 | 66 7 | 313 | 73 1 | | |
| Unsatisfactory No improvement Relapse Progression of ocular condition Counting fingers Light perception Blindness | 15 7 3 1 2 | 9 6 4 5 1 9 0 6 1 3 | 12 3 3 1 1 | 13 8 3 4 3 4 1 1 1 1 | 10 2 1 1 1 1 | 18 2 3 6 1 8 1 8 1 8 | 23 1 4 4 7 4 | 17 8 0 8 3 1 3 1 5 4 3 1 | 66 14 10 7 13 5 | 15 4 3 3 2 3 1 6 3 0 1 2 | | |
| Grand total | 28 | 17 8 | 20 | 23 0 | 15 | 27 3 | 43 | 33 3 | 115 | 26 9 | | |

^{*}The figures in this column refer to patients beginning treatment within two months of the onset of interstitial keratitis (Courtesy, Arch Dermat and Syph, April, 1937)

[†] This total does not include patients treated in the first two years of life or those for whom the age at the onset of interstitial keratitis was unknown (Courtesy, Arch Dermat and Syph, April, 1937)

and continuous administration of mercury or bismuth preparations and some accepted form of arsenical compound. Such therapy as the administration of iodides and foreign proteins had no advantages in the acute stages of keratitis but might be considered to be of some value in the later, chronic phases of the disease. The following charts indicate the results of treatment

Lesions of the cyc in older children with congenital syphilis are the most frequent symptoms of the disease. A thorough study of the syphilitic conditions of the eye was made with careful ophthalmological examinations of 143 syphilitic children of all ages, by V. E. Lennarson and P. C. Jeans 367. The eye was found to be involved in 66 per cent of the group. In infants under two years of age, eye lesions were comparatively rare although optic atrophy, chorioretinitis and interstitial keratitis were observed.

In children over two years of age, interstitial keratitis was the most common type of lesion, occurring in 43 per cent of the group, with the highest incidence in patients eight years of age. In three instances the interstitial keratitis developed within three weeks after adequate treatment of congenial lues had been instituted. In the group of older children chorioretimitis occurred in 13 per cent and optic atrophy in six per cent. Paralytic squint was noted in only two patients

The serologic tests were usually strongly positive in children with keratitis who had received little or no treatment but the lesion was also observed in those who had moderate or weak reactions. Other eye lesions than keratitis were usually accompanied by more strongly positive reactions of the blood and cerebrospinal fluid than was the average in the group as a whole

TUBERCULOSIS IN CHILDREN

By Waldo E Nelson, AB, MD

Clinical Manifestations—An additional argument against the use of the "epituberculosis," to designate retrogressive, consolidative, pulmonary tuberculous lesions is supplied by the case report of H C Cameron and S de Navasquez 368. An instance of a child who had a wedge-shaped consolidative pulmonary lesion and who later developed a terminal tuberculous meningitis is reported together with the pathologic The pulmonary lesion was shown to be a low grade tuberculous pneumonia and a few viable tubercle bacıllı were present The pulmonary lesion apparently originated from the rupture of a caseous bronchial lymph

node into the bronchus It was thought, but not proved, that the tuberculous meningitis also originated from this bronchial lymph node by erosion into a blood vessel. The important point in this report is the pathologic demonstration of a tuberculous lesion with viable tubercle bacilli in an instance when the roentgenographic diagnosis was that of epituberculosis This evidence is in line with that of Reichle and Oppenheimer (both previously reported in earlier supplements of the Cyclopedia of Medicine) and is evidence against the explanation of Eliasberg and Neuland that such lesions are nonspecific infiltrations would seem safer to consider all consolidative tuberculous lesions as tuberculous pneumonias, and to recognize that they may retrogress

Ten instances of chronic miliary tuberculosis in children are reported by R H Fish 369 Recovery occurred in four of these children The author believes that chronic miliary tuberculosis is more frequent than is generally recognized and recovery occurs in a fair proportion of the chronic cases Recovery is said to be commonest when the nodules are confined to the lungs However, it may occur in generalized cases and even when the onset is moderately acute Microscopic sections of the lungs in three of the fatal cases demonstrated that healing was taking place in some of the individual miliary nodules Healing proceeds by a process of fibrosis which usually results in roentgenographic disappearance of the nodules In the differential diagnosis the author points out the necessity of proving that the roentgenologic shadows are due to tuberculous processes and that the nodules result from the dissemination of tubercle bacilli by the blood stream Sımılar roentgenologic shadows in the chest may be produced by such diseases as pneumoconiosis, carcinomatosis, bronchobronchiolitis, pneumonia or vascular congestion due to cardiac insufficiency and disseminated blood following hemoptysis Bronchogenic distribution of the tubercle bacilli resulting m a tuberculous bronchopneumoma may also produce lesions which on the roentgenogram appear quite similar to those of miliary tuberculosis

Primary vs. Reinfection Tuberculosis

In regard to the question of distinguishing between primary and reinfection tuberculosis in childhood, H Casparis³⁷⁰ suggests that there would

be less confusion if tuberculosis simply be considered as tuberculosis, regardless of the patient's age. He points out that either the primary type of infection (so-called childhood tuberculosis) or the reinfection type (so-called adult tuberculosis) can occur at any age and that it is impossible to determine when the individual patient received his first infection, how many times he has been infected or what the size of each infection was The important factor is that the patient has received sufficient tubercle bacilli from some source and at some time to make him sick. He also states that the methods employed for diagnosing and treating tuberculosis in children are not fundamentally different from those that are employed for adults. In illustration, reference is made to the case of an infant, five months of age, who had pulmonary tuberculosis with cavitation and tubercle bacilli in the The involved lung was collapsed and the cavity obliterated by means of pneumothorax The collapse was maintained for a period of months and the child was apparently healthy three or four years later

Differential Diagnosis - The fact that pulmonary tuberculosis and bronchiectasis may be coexistent in children is pointed out by L B Dickey 171 The author reports two instances in each of which the two conditions occurred in the same child and probably independently of each other When bronchiectasis and tuberculosis occur together, it is more difficult to prove the existence of tuberculosis than of bronchiectasis In such an instance acid-fast bacilli occur in sputum considerably diluted by material from bronchiectatic cavities and detecting them is as difficult as in pleural fluid or in fluid from the spinal canal It is obvious however, that insistent search should always be made of the

concentrated material from bronchiectatic cavities, when there is a definite history of tuberculosis or tuberculous contact. The recognition of tuberculosis in persons suffering from bronchiectasis is important from a public health standpoint. These persons are potential, if not actual, disseminators of tubercle bacilli and the hazard exists in the fact that bronchiectasis, which might predominate the clinical picture, is not generally considered to render the patient a danger to society.

1050

A study of the basal metabolism of tuberculous children has been made by A Topper and H Rosenberg 372 They found that children with an active childhood (primary) type of tuberculosis have an increase in basal metabolism even in the absence of fever, while children with an active afebrile adult (reinfection) type of tuberculosis tend to have a normal metabolism While the authors admit that the explanation of this difference is not clear, they suggest that the cause probably is in the pathologic and immunologic differences inherent in the two types of infection. Thus they raised the following questions (1) Is the dynamic power of lymphatic tissue greater than that of other cellular tissue? (2) Is the intensity of reactivity greater during the childhood type of infection than during the adult type? They point out that in diseases of the lymphatic system, notably leukenna, a high basal metabolism is found even in the absence of fever It is also pointed out that the intensity of skin reactions to tuberculin are less marked in adults than in children

Tuberculin—Further studies on Purified Protein Derivative of Tuberculin (P P D) are reported by E R Long and F B Seibert. ⁸⁷⁸ Data have been collected from various parts of the country which support the original contention

that P P D is an adequate testing medium. With few exceptions, patients with clinical tuberculosis react to the Purified Protein Derivative, and a great majority of them react to the first or smaller of the standard doses (0 00002 mg). The exceptions were for the most part patients with acute tuberculosis or seriously ill patients with chronic tuberculosis of long standing A small number of persons with calcified tuberculous lesions from first infection did not react to the Purified Protein Derivative or other forms of tuberculin

Evidence is presented which indicates that some of the reactions to the second dose of Purified Protein Derivative (0.005 mg), in instances in which reactions to the first dose were negative, may be non-specific. This statement also applied to other forms of tuberculin Reactions to the second dose were elicited equally well by large doses of analagous protein derivatives from other acid-fast bacteria. This appears to be a non-specific effect, since small doses of the latter protein derivatives did not cause reactions in subjects highly sensitive to Purified Protein Derivative of the tubercle bacıllus Means are not available at the present time for distinguishing specific from non-specific reactions

There is a demand for a single dosage of tuberculin which will detect all of the clinically significant cases and all of the significant contact cases, and at the same time not cause a high percentage of severe reactions. Some advance has been made in selecting such an intermediate dose. It is emphasized, however, that the basic dose will vary, for different parts of the country, where differences of tuberculinization of the population prevail, and for different social groups in the same locality. In communities where less than 40 per cent react to the two doses (0 00002 mg and 0 005 mg),

a dose 1/10 as large as the standard second dose, namely, an intermediate dose of 0 0005 mg appears practical for case finding purposes and surveys for significant contacts. It must be realized, however, that there are certain disadvantages in the use of such a dosage of tuberculin A small per cent of the less sensitive tuberculin reactors will be missed and, on the other hand, a greater number of exceptionally strongly positive reactions will be obtained than with the initial use of 0 00002 mg. of P P D. The real test would seem to depend upon whether it can be shown that such a dose (0 00005 mg or such other intermediate dosage as may be determined upon) will detect practically all of the clinically active cases of tuberculosis The authors also submit evidence to show that dilutions of Purified Protein Derivative may be kept somewhat longer than has been stated previously practical purposes it seems safe to keep the standard dilutions of P P D three days in the icebox. Thus it is necessary to make fresh dilutions only twice a week

A study designed to determine whether there is any relation between the intensity of the tuberculin reaction and the presence of demonstrable tuberculous lesions has been conducted by C W Wells and H H Smith 374 Their data are based upon the tuberculin reactions and roentgenologic examinations of 4,906 persons They found a distinct upward trend in the percentage of demonstrable tuberculous lesions, both latent and manifest, with increasing severity in the tuberculin reaction In the 0-9 year age group, the percentage of demonstrable tuberculous lesions ranged from 05 per cent for negative reactors to one mg of tuberculin to 141 per cent in the 2, 3 and 4 plus reactors to 001 mg of tuberculin In the 10-14 year age group

no lesions were found among the negative reactors and 142 per cent of tuberculous lesions in the 2, 3 and 4 plus reactors. Among those over 15 years of age, there were 55 per cent of tuberculous lesions among the negative reactors and 121 per cent in those who had 2, 3 and 4 plus reactions to 001 mg of tuberculin. This study does not answer the important question, whether active tuberculous lesions can be distinguished from mactive ones by the intensity of the tuberculin reaction, since practically all of the tuberculous lesions among the children were classified as latent. In the group over 14 years of age there was no significant difference in the ratio of active pulmonary lesions to latent ones among those who had weakly positive or strongly positive tuberculin reactions It would seem from this study that the intensity of the reaction to tuberculin in the amounts used by the authors is not a reliable method for determining activity of tuberculous lesions. If there is such a relationship, it would seem more likely that it would be demonstrated by much weaker tuberculin solutions were employed by D. Ayman 375

Additional evidence has been presented by W E Nelson, F B Seibert and E R Long,376 which emphasizes the heat stability of tuberculin and the tendency of tuberculin to remain adherent to glassware and rubber after cleaning and sterilizing by the ordinary methods They have shown that a certain proportion of tuberculin-positive subjects react to the injection of physiologic solution of sodium chloride from syringes previously used for tuberculin and then simply washed and sterilized Tuberculin may also be introduced into supposedly tuberculin-free mediums by the use of pipettes and rubber stoppers, previously employed for tuberculin and subsequently cleaned by the ordinary methods The

clinical importance of these facts is apparent When Schick tests were made with syringes previously used for tuberculin and cleaned by ordinary methods, falsely positive Schick tests, in reality tuberculin reactions, were often obtained The danger in the employment of tuberculin syringes in routine allergy tests as with pollen protein is also pointed out The most effective methods of cleaning syringes to destroy all traces of tuberculin were found to be boiling in soap solution and prolonged immersion ın sulfuric acid-potassium dichromate cleaning fluid. It is safer and more practical, however, to keep separate syringes for tuberculin, Schick and the various protein allergy tests, and to mark them in such a manner that they will not be confused with one another and used interchangeably for these various tests

Prognosis-For a period of one to five years, M Brailey377 has followed a group of 170 children who were found to have a positive tuberculin reaction before the age of two years. At the time of the initial roentgenographic examination, 67 of these children had demonstrable parenchymal involvement of the lungs and 103 of them had no demonstrable parenchymal lesion. The total five year mortality for white children was 13 per cent and for the colored children 31 per cent Approximately 70 per cent of the deaths occurred within the first year after the discovery of infection and most of these within the first six months. The mortality was 31 per cent within the first year of observation of those children who had involvement of the lung parenchyma In this group there was no difference in mortality between the two races Among those whose initial chest plates showed no parenchymal involvement, mortality during the first year subsequent to the discovery of infection was 68 per cent No death occurred among the 49 white children of this group, but there were seven deaths among 54 colored children. In both white and colored children, the mortality was more than twice as high in those known to be infected during the first six months of life, as in those whose infection was discovered between the ages of six months and two years

Immunity—In view of the present controversy regarding the degree of immunity or lack of it conferred by the primary infection with the tubercle bacillus, the discussion of H S Reichle and M Gallavan378 on the acquired required resistance to tuberculosis is of The authors have carefully studied the postmortem findings in 87 cases of tuberculosis with the idea of testing the validity of Ranke's classifica-(1, the primary focus, 2, the spreading of the bacilli and, 3, tertiary lesions of an organ or of an organic system) and his concept of a blockade which, developing in the course of a primary infection, localizes all subsequent lesions. Such an obstruction is spoken of as the lymphatic or the hematic blockade Evidences of lymphatic blockades were demonstrated in 45 of 73 cases of reinfection tuberculosis, and in 49 of these cases the evidence indicated an hematic blockade. In the discussion of their observations and the experimental results of other workers, the authors state that the evidence favors the assumption that a person does acquire some resistance in the course of a primary infection and that the changed status of cells or of body fluid is sufficient to alter favorably the reaction of the body to reinfection. The immunity in tuberculosis, however, must be considered to be of a lesser degree and probably of an entirely different character from that of such diseases as measles and smallpox The degree of resistance to tuberculosis is not sufficient to prevent the development of clinically apparent disease in organs whose preexistent channels of communication, such as the bronchi of the lung and the tubes of the genito-urinary tract, are avenues by which the disease is easily diffused

In such instances destructive disease occurs, the forces of resistance, however, are sufficient to prevent spread beyond the organ attacked Blockades cannot be purely mechanical, as would be produced by obliteration of the lymphatic system and fibrosis of the nodes Lymph, inflammatory exudate and tubercle bacıllı do reach the nodes Tubercle bacıllı, however, have been demonstrated in the blood stream of persons suffering from active tuberculosis It must therefore be assumed that the bacilli pass in relatively large numbers from the lesions in the lung into the nodes and the blood stream, where, however, they are destroyed or succeed at the most in producing small proliferative and not progressive lesions Naturally, as a terminal event, a break in the blockades may occur Immunity in tuberculosis is therefore largely the result of localization of the disease must not be assumed that such localization necessarily leads to a cure On the contrary, as in meningococcic infections, the very localization may lead to a fatal though localized disease

Further studies have been carried out by B J Clawson³⁷⁹ to determine what relation, if any, exists between allergy induced by a primary tuberculous infection (Ghon tubercle) and immunity to reinfection tuberculosis. There is no agreement at the present time upon the question whether a primary healed pulmonary lesion with associated allergy should be considered a useful or a harmful factor in relation to reinfection with the tubercle bacillus. There are two

schools of thought The first group emphasizes the harmful effects of allergy caused by the existence of the Ghon tubercle Immunity, if present, is believed to be almost masked or overcome by the bad influence of allergy This is illustrated by the statement of C A. Stewart,380 "The relationship existing between the childhood and adult types of tuberculosis seems to consist largely in the tendency for the primary infection to prepare the patient for the development of phthisis should he perchance later experience a reinfection of sufficient severity to produce an intrapulmonary lesion." The second group of investigators are convinced that a degree of immunity is associated with nonprogressive primary tuberculosis Allergy, while admitted to have a harmful aspect, such as responsibility for an increased degree of necrosis, should not be taken too seriously It is sometimes stated that without allergy there is no resistance In proof of this statement the fact is cited that the greater number of persons who have a Ghon tubercle do not later develop clinical tuberculosis even though exposed to repeated infections

Clawson has studied this problem in rabbits Using the B C G strain of tubercle bacıllı, Ghon tubercles were produced in the lungs of rabbits. His experiments showed that rabbits which were allergic had a marked degree of resistance to subsequent infection with a virulent strain of tubercle bacilli. This resistance was not dependent on allergy alone, since he had shown in previous experiments that resistance could be developed as well by a method in which allergy did not occur He has also shown that allergy can disappear to the extent that no positive cutaneous reaction is elicited by an intracutaneous injection of 1 mg of old tuberculin, and the animals maintain a high degree of resis-

tance against virulent infection. Clawson suggests that the fact that allergy occurs so early in the development of tuberculosis does not support the theory that the factor causing the severe secondary or adult type of pulmonary tuberculosis is allergy, since apparently all tuberculosis, both the childhood and the adult type, even before it can be observed anatomically or clinically, is associated with and influenced by allergy These experiments present strong evidence that a marked degree of resistance, even in the presence of allergy, may be developed from primary pulmonary infection (Ghon tubercle) The author states emphatically that his purpose in these experiments is not to recommend a method of vaccination against tuberculosis but to suggest, on the basis of a comparative study, the prognosis of pulmonary tuberculosis from the standpoint of the influence of the factors of allergy and resistance in a person with a healed or an arrested Ghon tubercle

Vitamin C In view of the attention directed at present to therapeutic administration of vitamin C to tuberculous patients the experimental study of F H Heise and G J Martin 181 is of interest In their experience supervitaminosis C maintained for a period of five months did not protect guinea-pigs against subcutaneous injection of 300,-000 virulent human tubercle bacilli

M M Steinbach and S J Klein³⁸² have studied the effects of crystalline vitamin C (ascorbic acid) on the tolerance to tuberculin of tuberculous guineapigs. Ascorbic acid mixed *in vitro* with skin test doses of tuberculin prior to intracutaneous inoculation in tuberculous guinea-pigs failed to inactivate the tuberculin in tests on 12 animals. Nor did prolonged treatment of seven tuberculous guinea-pigs with ascorbic acid reduce the activity of the skin to small doses

of tuberculin. They were also unable to determine any ability of the vitamin to inactivate tuberculin either in vitro or in vivo when the tuberculin was used in a dose large enough to cause death of control tuberculous guinea-pigs. When, however, the tuberculin was injected in somewhat smaller but repeated doses large enough in the aggregate to be fatal to control tuberculous animals, it was found that administration of ascorbic acid usually resulted in survival of the animal

Prophylaxis-An analysis of the experience with B C G vaccination in the various European countries has been completel by G G Kayne 383 On the basis of this survey he concludes that B C G is harmless and that it confers a partial immunity which is effective only if combined with other methods of prophylaxis This partial immunity apparently is of short duration, lasting only six to 12 months. He enumerates a number of factors which he considers essential for the rational application of $B \ C \ G$ These are as follows (1) The vaccine should be of a standard strength (2) Methods for detecting small differences in the strength of the vaccine should be perfected (3) The preparation of the emulsion and the date of use should be such as to insure a more or less constant number of living bacilli at the time of administration (4) A suitable route of administration should be employed Parenteral injections, intracutaneous or subcutaneous, are recommended (5) A dose of vaccine should be used which will produce tuberculin hypersensitiveness as rapidly as possible with the least inconvenience (6) The vaccinated child should be protected from tuberculous infection until a positive tuberculin reaction is obtained after the vaccination (7) Only children who must remain in contact with open tuberculosis should be vaccinated It is the Reviewer's opinion that B C G vaccination should be employed only when all of these factors can be satisfactorily accounted for and when there is ample opportunity for following all of the vaccinated children and an adequate control group. It would seem not unwise to depend upon the children already vaccinated for the test of the efficacy or the lack of it and defer further vaccination until more and complete data of the late effects of vaccination with B C G are available

C Kereszturi and W. H. Park³⁸⁴ have also reviewed their experience of the past eight years with the use of B C G vaccine as a prophylactic against tuberculosis in children They have no evidence to indicate that $B \ C \ G$ is harmful to animals or to man They favor the parenteral administration of the vaccine rather than the oral, since in their series the death rate from tuberculosis in those children vaccinated by the parenteral method was one-fourth that of the non-vaccinated control group, whereas in the orally vaccinated group the death rate from tuberculosis was only one-half the control group It is their opinion that B C G can now be used as a public health measure for the prevention of tuberculosis in those who have not yet become infected and who may be exposed later to tuberculosis in their own families They do believe, however, that further data should be collected in regard to the efficacy of the vaccine in several well equipped centers with adequate control groups Unfortunately, the differences in the death rate from tuberculosis between the orally vaccinated, the parenterally vaccinated and the control non-vaccinated groups are not statistically significant and while the differences in mortality in the several groups may be due to the B C G vaccination, this cannot be supported from the data presented by the authors and further analysis of this nature in larger groups is necessary to establish beyond doubt the efficacy of B. C G

Treatment-It has been stated by Myers and Stewart that there is no need for unusual restriction of activity of children with primary intrathoracic tuberculosis and in particular that there is no need for preventorium care This attitude, however, is not universally accepted J A Johnston385 believes that the low mortality of tuberculosis in his group of 650 positive tuberculin reactors over a period of seven years justifies the existence of the preventorium plan and in this respect is in agreement with Hawes. During this period of observation there were only two deaths, each from miliary tuberculosis Twenty-three instances of reinfection tuberculosis were discovered Sixteen of these developed subsequent to the initial observation Since in only two of these was there any question of reexposure, the author believes that this is evidence in favor of endogenous reinfection

A follow-up study of ambulatory children with tuberculous infections is reported by E Wolff and S Hurwitz 386 The average period of observation was seven years The initial and subsequent examinations included tuberculin tests and complete physical and roentgenological examinations There were 162 children who were followed throughout the period of study Clinically, all patients, with four exceptions, are now perfectly healthy These latter children belong in a group of eight who had continued exposure In the entire series there was but one death, this was caused by tuberculous meningitis. The roentgenologic findings became negative or latent in 98 per cent of all cases In 12 per cent there were active lesions at the time of the initial examination, these diminished to

two per cent at the last recheck The majority of patients with doubtful roent-genographic shadows at the commencement later revealed evidence of latent tuberculous processes. It is the author's impression that the subsequent course of the disease in ambulatory children with pulmonary tuberculous infection is extremely favorable provided that they are adequately supervised and that they are not exposed to reinfection.

In a discussion of home versus preventorium care in the management of tuberculosis contacts, L J Moorman387 points out that even though the results warranted an all inclusive preventorium program, the cost would be prohibitive In view of this and the fact that in the preventorium plan the good results are dependent upon the family program, it would seem wise to consider the comprehensive dispensary scheme which, in addition to case finding, family supervision, and family and community education, is definitely committed to the breaking of contacts by removal of the patient from the home rather than by removal of the exposed child. It would then seem advisable to devote available beds to the more or less permanent residence for those children in homes where it is impossible to break contact or to improve environment, and to the temporary residence of those in homes where contacts may be broken but where time is required to affect the removal of the patient from the home. In order favorably to influence environment in a permanent and effective manner, the efforts must be directed at the home. The child who helps to work out successfully the family program under existing financial and environmental handicaps will learn to appreciate the value of individual effort, the necessity of family responsibility, the need of community service,

and the obligations of good citizenship In addition to all these factors, he will have an equal chance with the preventorium child to escape manifest tuberculosis providing, of course, that the active cases of tuberculosis are removed from the home

The need for more extensive use of compression therapy by means of artificial pneumothorax, phrenicectomy pneumolysis or thoracoplasty in the treatment of children with the adult type of active pulmonary tuberculosis is emphasized by M Gross and S B English 388 It is pointed out that juvenile patients do not fare well when harboring the adult type of tuberculosis, and further that tuberculosis is the main cause of death in juvenile patients Routine bed rest, together with high vitamin diet, has not proved satisfactory in lessening the mortality rate The importance of early diagnosis is emphasized and also that as soon as the reinfection type of tuberculosis is evident, compression therapy should be instituted immediately The authors prefer the use of artificial pneumothorax and have obtained the best results in those patients in whom a free pleural space could be found and adequate collapse obtained If proper and adequate compression cannot be obtained by this method, then phrenic crushing may be employed Pneumolysis may be employed in selected cases. The authors have had no experience in the use of thoracoplastic surgery in juvenile patients However, they suggest that it should be considered as a possible means of securing collapse of the lungs when other methods fail Bilateral, artificial pneumothorax may be performed when indicated

Children with positive sputum should be separated from those with negative sputum since cross infection may occur Since some of the children who have been sputum-positive before the institution of collapse therapy become sputumnegative after treatment, they should be removed from contact with the sputumpositive children as soon as they become sputum-negative H Starcke³⁸⁹ advises against active diphtheria immunization in children with active tuberculosis. He points out that the tuberculous lesions may be reactivated and the child may be more susceptible to other intercurrent infections due to a loss of resistance

WHOOPING COUGH

By ROBERT A LYON, A.B, A.M, MD

The use of pertussis vaccine continues to show promising results provided that the child is immunized early, the best age being 7 to 12 months

Immune blood is believed to contain antibodies against whooping cough and when given early in the incubation period of the disease it has been effective in modifying or preventing the symptoms

Very little attention has been paid in the past to the changes produced by whooping cough on certain chemical constituents of the patients' blood The relation of the acid-base equilibrium to the pathogenesis of whooping cough has been investigated recently by J C Regan and Tolstoouhov 390 Their results indicated that pertussis in its early stages usually increases the hydrogen ion concentration of the blood without showing any variations beyond normal limits of the carbon droxide combining power Inorganic phosphorus and sugar levels in the blood are usually lowered and the uric acid content is elevated The condition of impending or real acidosis iii pertussis patients was thought to be due to an interference with normal respiratory exchange of carbon dioxide and oxygen Such respiratory difficulties arise from pathological changes in the lung tissue, the paroxysmal cough and the fatigue of the respiratory mechanism Vomiting was considered to be a symptom of acidosis but was rarely carried to such an extent that it produced an alkalosis by removal of the HCL from the body. The deprivation of food in pertussis patients may aid in causing acidosis. The authors were inclined to believe that the administration of alkali and provision of adequate amounts of fresh air and oxygen were distinctly beneficial in relieving the acidosis and in stimulating respiratory function.

Diagnosis - Many difficulties have arisen in making an early diagnosis of whooping cough by the laboratory procedures which are available The subject has been reviewed recently by A E Gold and H O Bell³⁹¹ in respect to the sedimentation rate and the blood cell count in such patients. In a small group of children in the early catarrhal stages of the disease, the sedimentation rates were slightly accelerated but not much different from that of acute respiratory infections in general. The white cell counts were unreliable with a relative lymphocytosis occurring in only about half of the number of patients. In later stages of the disease, after the paroxysmal cough has developed, the white cell count was of more value in diagnosis because of the elevation of total numbers and especially of lymphocytes in the majority of cases The sedimentation rates at that time were generally re-

tarded As the disease subsided, the sedimentation rates were slightly accelerated and the blood counts tended to revert to normal The occurrence of complications was reflected by increased sedimentation rates and elevated polymorphonuclear counts with a slight shift to the left, as determined by the Schilling index It was the conclusion of the authors that during the early stages of the disease the cough plate method was the best procedure for the diagnosis of whooping cough, but in later stages the sedimentation rate and the blood cell count aided in the detection of complications of the disease The diagnostic value of complement fixation tests, agglutination and cutaneous reactions were questioned by the authors but all diagnostic laboratory tests may be employed with profit, if one bears in mind their relative value in the various stages of the infection

Employing three methods of diagnosis, the white cell and differential counts, agglutination tests and complement fixation reactions, L Daughtry-Denmark 192 found the last test the most accurate A leukocytosis consisting chiefly of an increase in the number of lymphocytes occurred fairly early in the course of the disease but the absence of a typical leukocytic response did not always exclude the diagnosis The administration of Sauer vaccine caused a lymphocytosis and the reaction of the cells was greater after giving double strength vaccine Agglutination tests did not prove to be specific for whooping cough Complement fixation reactions, with the pertussis bacillus employed as the antigen, were positive in 94 per cent of a group of 56 children with whooping cough a week before the typical paroxysms developed, and in 100 per cent of the group during the first week of the whooping stage Only a small percentage of convalescent patients and normal young adults who had had whooping cough in childhood had positive complement fixation reactions, but positive reactions, but positive reactions, but positive reactions could be produced in children of all ages by the injection of Sauer vaccine. When vaccine of double strength was administered to 100 children, complete complement fixation developed rapidly

The complement fixation test for pertussis has met with various degrees of success in the hands of different investigators One of the chief reasons for the differences in results, according to M Weichsel and H S Douglas³⁹³ was the difficulty in obtaining pure strains of pertussis bacilli In reviewing the accuracy of the test, the authors found that infants under one year of age who were suffering from whooping cough frequently did not develop antibodies to produce a positive complement fixation reaction, but older children gave positive results in 80 per cent of cases after the second week of the disease and remained positive for five to eight months normal children the tests were negative in 90 per cent of instances regardless of a previous history of having or of not having had the disease Children who had received pertussis vaccine shortly before the development of whooping cough usually developed strong complement fixation reactions within a relatively short time after the cough began Normal adults gave positive reactions more frequently than children, regardless of their histories of previous infections Doctors and nurses who were exposed regularly to the disease were no more apt to give positive reactions than ordinary groups of adults Tests of the antibodies in these adult groups indicated that they were of a specific nature, but no explanation could be found for the higher incidence of positive complement fixation reactions in adults. The cord blood of infants contained antibodies in definite relationship to those found in the blood of their respective mothers and the authors concluded that the amboceptors could pass through the placenta

The association of acute lymphatic leukemia with whooping cough offers many difficulties of diagnosis In the patient reported by W Levy, M J H. Grand and S. A Krakauer³⁹⁴ the two conditions occurred simultaneously The symptoms and the marked response of lymphocytes in both diseases are much the same but in leukemia more immature forms of lymphocytes occur in the blood and there is not the complete remission to normal conditions as in pertussis In the reported case of a seven-year-old boy, pertussis was diagnosed by the cough plate method, but the presence of 230,000 white cells, of which 97 per cent were lymphocytes, and the marked enlargement of the liver and spleen suggested the presence of leukemia The successive blood counts showed some remission in the number of lymphocytes but the child's condition grew rapidly worse in spite of transfusion and other therapeutic procedures The authors stressed the importance of making repeated examinations of the blood of patients with pertussis who have a marked leukocytosis and whose progress does not simulate the general course of whooping cough

Treatment — The results obtained from the *vaccine* treatment of whooping cough patients are hard to judge because of the natural variations which occur in the course of the disease J J Miller, Jr, and C Singer-Brooks³⁹⁵ have compared the pertussis infections of a treated and a control group and found very few differences in the duration or severity of the infection Twenty-eight children, varying in age from seven weeks to

seven years, received various amounts of pertussis undenatured bacterial antigen, 17 of them after the paroxysms of the disease had begun, ten during catarrhal stages and one before any symptoms had begun Of the 17 children in the control group, some were brothers or sisters of the treated patients. The severity of the disease was judged by the number of paroxysms during a 24-hour period, the day on which the maximum number occurred, the number of times the child whooped or vomited, the length of each stage of the illness and the development of complications. Marked variations in the type and severity of pertussis occurred in both the treated and in the control group but no definite effects attributable to the vaccine injections could be observed. The authors suggested the possibility of obtaining better results from more numerous injections of a potent material but doubted whether sufficient benefit could be obtained to make such a procedure practi-

The vaccine treatment of active, infectious pertussis had little or no effect in altering the course of the disease of a group of patients observed by T S Bumbalo ³⁹⁶ Employing the New York State pertussis vaccine, the author treated one child and left untreated another child of the same family A comparison of the course of the disease, the complications and mortality rates of 447 such patients showed no beneficial or harmful effects of the vaccine

When the vaccine was employed to produce active immunity to the disease, the results were questionable. Pertussis was contracted by as great a percentage of the immunized group as of the non-treated group but milder forms seemed to occur in those who had protective vaccine injections.

If vaccine therapy is of value in only a small number of patients, the procedure should not be discarded entirely was the opinion of W Keller 397 From the observation of the complement fixation reaction, the author noted that the antibodies produced by the vaccination and those produced by the disease were the same in general character Children treated with vaccine after the cough had begun, developed antibodies more rapidly than did untreated children Administration of the vaccine after the titer of antibodies had risen to its peak did no good in shortening the course of the disease The therapy likewise had no beneficial action on complications of the illness The author emphasized the fact that the vaccine therapy may be of value in some patients when it is administered early enough in the course of the disease

A modified type of vaccine has been prepared recently by J A Toomey 398 He employed the mucoid material produced by cultures of phase I pertussis hacilli diluted with normal saline solution so that each cubic centimeter contained 40 mg of the mucoid material Results obtained from the treatment of 80 children under three years of age in the early stages of whooping cough have been reported as successful. This work is still in the experimental stage but it was thought by the author that this mucoid material produced by active organisms resembled in many respects the mucoid material coughed up by the patient during active stages of the disease, and that the resistance or immunity of the patient might be in definite relationship to the disappearance or overcoming of this mucoid production

Considerable attention has been given during the past year to the treatment of children with whooping cough by the administration of vaccine by the intra-

nasal route The material employed was the soluble substance derived from cultures of the pertussis bacillus representing 20,000 million organisms per cubic centimeter H A. Slesinger³⁹⁹ instilled ten drops of the antigen into nostrils every day or every other day for four to 12 treatments In the observation of 24 active cases of whooping cough, 46 per cent showed considerable improvement, and 29 were moderately improved, as judged by the number of paroxysms and the duration of the disease The material was given to three children who had been exposed to whooping cough and two of these patients subsequently developed mild symptoms, and one child escaped the disease entirely

Encouraging results from the intranasal treatment of pertussis patients have also been reported by H Gold 400 The material was instilled in each nostril daily in amounts of five to ten drops depending upon the severity of the symp-The paroxysmal stage was definitely shortened or reduced in severity in 86 per cent of a group of 28 cases In two other children the nasal treatment was started two weeks after symptoms of the disease developed and it seemed to prevent the development of the paroxysmal attacks, but the symptoms of the catarrhal stage or other respiratory symptoms were not relieved by the medication. It was the opinion of the author that the vaccine acted as a desensitization form of treatment

The administration of ether per rectum has been a form of treatment of severe pertussis infections which has met with varying success in the past A recent favorable report of this type of therapy has been made by N Leone Bloise and E Alvariza Berez 401 The solution employed consisted of 5 drams (20 cc) of a ten per cent solution of

camphor in ether, 1 oz (30 Gm) of eucalyptol and 3½ oz (100 cc) of a four per cent solution of aromatized oil in liquid petrolatum. Doses of 1 to 4 drams (4 to 16 cc), depending upon the age of the child, were instilled into the rectum daily for 8 to 15 days, depending upon the severity of the infection. Judging from the severity of the attacks and the number of complications, the authors concluded that 80 per cent of a group of 80 patients with pertussis received considerable benefit from the treatment.

Prevention—Several controversial points remain in regard to the methods of preparation of prophylactic pertussis vaccine Among these are the relative values of stock cultures of the organism and freshly isolated strains, the type of medium most suitable for growing the organism, and the necessity of adding of human rather than sheep's blood to the medium. These subjects have been discussed in a recent review of the subject by L Mishulow, I Mowry and R Orange 402 They employed the agglutinin response as a measure of the effectiveness of vaccine administration maximum agglutinin response was never found to be as high in vaccinated children as in those who had exeprienced the disease itself but in general, the reaction followed the same course and duration in both types of children Vaccines piepared from stock cultures grown on sheep's blood infusion agar and retaining the toxin materials of the culture growth, stimulated a better agglutinin response than did the vaccine prepared, according to the Sauer method, from freshly isolated cultures grown on human blood Bordet-Gengou media depended considerably upon the dosage of vaccine, and a total number of 80 billion bacteria seemed to be necessary to stimulate a maximum response in 84 per cent of the group The intracutaneous method of administration of the vaccine stimulated agglutinin production with a smaller dose than was needed by the intramuscular route but reactions were often more severe by the former method When the vaccine was administered at two-day intervals a better response was obtained than when it was administered at seven-day intervals

The vaccine prepared by Mishulow contains ten billion pertussis organisms per cubic centimeter and includes a small amount of a toxic substance capable of giving a Schwartzman reaction in rabbits This vaccine is prepared by the Sauer method except that stock bacilli were employed and were grown on a medium containing normal animal blood instead of human blood Favorable results have been obtained with this vaccine in a group of 74 children inoculated by E Y Shorr 403 Only 16 per cent of this group contracted pertussis while 36 per cent of an untreated group developed the disease during the same period of time. In a small number of patients in whom the agglutinin response was studied, the titers were found to rise rapidly during the first month after treatment and to Attempts were fall rapidly thereafter made in a group of children to administer the vaccine by the intracutaneous route but it was found impossible to administer a sufficient quantity to afford protection and the reactions were more severe by this method The agglutinin response, however, was more sustained and lasted a longer period of time It was the conclusion of the author that the Mishulow vaccine administered in amounts of 65 billion bacilli, afforded protection for the majority of children and compared very favorably with the Sauer vaccine The additional advantage of its being produced from stock strains of bacilli and grown on culture

media not requiring human blood made preparation easier and less expensive

Less striking results with prophylactic vaccination of children against whooping cough have been reported by J A Doull, G S Shibley and J E McClelland 404 Vaccine prepared from five freshly isolated strains of the pertussis bacillus grown on human blood agar was employed in the treatment of a group of 483 children The dosage was 8 cc given in three doses and a total of about 80 billion organisms were administered A control group of about the same number of patients was observed during ten periods of 12 weeks each During this time whooping cough developed in 61 of the treated group and in 71 of the untreated series The severity of the infection seemed a little greater in the untreated group and the only death occurred in a child who had not received the vaccine The authors were inclined to doubt somewhat the value of the preventive therapy

Human convalescent serum has proved of value in the prevention of whooping cough if administered at least six days before the onset of symptoms. F M Meader⁴⁰⁵ injected a group of 94 susceptible children under seven years of age with 10 cc of pooled serum obtained from patients who had recently recovered from whooping cough About 72 per cent of the group seemed to be protected from the disease when the expected incidence rates of control groups are used as comparison The long incubation period of whooping cough makes the use of convalescent serum for protective purposes more difficult and the results less spectacular but the author believed that the intelligent ad-1.11n1stration of it would be distinctly beneficial, especially for children of the vounger age groups

JUVENILE DELINQUENCY

By Robert A Lyon, M D

A review of 3281 delinquent children who passed through juvenile courts of 60 Pennsylvania counties in 1932 was made by B S Alper and G E Lodgen 406 Delinquency occurred in larger proportions in the more populous counties than in the rural ones and more than three times as many boys as girls were apprehended Property crimes were the most common offenses among boys and the majority of girls reached court because of sex difficulties An interesting finding in this study was the greater tendency for rural districts to commit their patients to institutions while the more populous districts resorted to probation more frequently Boys were sent to institutions more often than girls, but there

was a general lack of uniformity in the various districts of the state in the manner in which patients were treated

Contributing Factors — In every large group of juvenile delinquents there are usually some patients with distinct psychotic tendencies. Among the series of 400 delinquents reviewed by W B Osgood and C E Trapp, 407 there were eight children with psychoses who had hallucinations, heard voices or were paranoid in their actions. An additional number of 14 had psychopathic personalities and two were epileptic. The average mental status of the entire group corresponded with that found in other studies in that it tended towards the low normal levels. The importance of the

home conditions in contributing to delinquency has been stressed in previous studies but the survey of the homes and families of this group of 400 delinquents did not indicate any preponderance of bad conditions, and approximately the same number of delinquents had come from normal homes as had come from homes of poor quality. The age and sex distribution of this group of delinquents and the types of crimes committed corresponded to the usual findings in such studies 408

Among the many factors which may be responsible for the development of delinquency in children is the broken home The broken home has been defined by R G Gordon⁴⁰⁹ as any situation which disturbs the normal relationship between father, mother and children and may be caused, therefore, by the absence of one or both parents because of divorce, separation or death, the presence of stepparents or step-children, or the division of a child's time between two homes such as that of the parents and that of grandparents or other relatives The authors cited five case histories in the majority of which the poor home conditions seemed to contribute to delinquency or abnormal behavior Other factors, however, which played important parts in the explanation of asocial conduct of these children, were mental retardation and physical defects The facilities for the treatment and prevention of juvenile delinquency in England are foster homes, voluntary homes and residential schools author favored placement in a foster home as the best method of removing a child from his original poor home conditions, providing the child was sent at an early age and the new parents were of satisfactory caliber Such new homes could hardly be expected to be ideal when the foster parents accepted such responsibility only because of the monetary reward and the better types of parents refused to take such children into their homes Commitment of juvenile delinquents to institutions was usually carried out through the courts most children had shown anti-social tendencies for considerable time before they committed a crime of sufficient severity to be brought to court, this form of treatment was usually begun too late in the child's life. When a contributing factor towards delinquency is found to consist of poor environmental conditions home, action must be taken early to improve the child's environment and relationship to his family

A comparative study of the factors influencing delinquency in 121 boys born in this country of native parentage and in 461 native boys of foreign parentage has been made by E T Glueck 410 Although the parents born in foreign countries, usually Italy, Ireland, Russia or Poland, had not received as much school training as the native parents, their economic status was about the same and the percentages employed in skilled trades were comparable There was a greater tendency for native-born parents to enter clerical or public service types of work, while more of the foreign born conducted private businesses of their own Overcrowding was more common in the homes of Italian parents Marriages and homes were more stable, certain moral standards were higher in the foreign parents, and the emotional ties between parents and their children seemed greater in this group

The children of these two groups of parents resembled each other in respect to the incidence of emotional or mental abnormalities. About 42 per cent of each group were above the average intelligence levels and about 25 per cent fell

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into the dull class. The amount of school training, retardation, the necessity for early withdrawal from school, and employment in street trades was similar in both groups. The boys of foreign born parents entered upon their delinquent acts at slightly earlier ages than the others.

A comparison of girl delinquents from native and foreign born groups indicated many of the same characteristics as in the case of the boys However, there seemed to be somewhat worse environment conditions and less parental supervision of the girls of foreign born parents than of native parents Considering all of the factors of likeness and dissimilarity between such groups, the author concluded that the balance of favor was towards the conditions in the homes of foreign born parents At least, there was no evident reason why native born children of foreign parents should become delinquent in greater proportions than in any other group, and the many efforts of social organizations in attacking the conditions and customs of the foreign born might be considered to be unnecessary and even haimful

Endocrine Disturbance - The role played by an endocrine disturbance on the behavior of an individual has been difficult to determine. The incidence of such abnormality was 17 per cent in a group of 2,311 delinquent children observed by N M Taylor and R L Schacter 411 It has been estimated previously that only about seven per cent of the general population exhibit endocrine disturbances so that the incidence among delinquents is distinctly elevated Boys and girls were affected in about equal proportions Pituitary involvement was observed more frequently among boys and its most common manifestation was dwarfism In girls, thyroid disturbances with hyposecretion were diagnosed most frequently. The incidence of abnormal gonadal conditions in boys was explained on the basis of the relatively greater ease of making a diagnosis in this sex. The great rise in the incidence of behavior problems at the age of puberty added weight to the probability that endocrine disturbance might have considerable influence on behavior at that period of life 412

Characteristics of Prisoners - In summarizing the characteristics of prisoners of today, S Bates413 stated that their average age is 26 years, more of them are married than single, and the majority come from the white native The southern states born population supply more in proportion to population than the northern ones Without question the majority of the juvenile delinquents and criminals come from social surroundings which are not proper, and the improvement of such conditions has been very slow and very madequate The average intelligence of the prisoner group is slightly above that of the average population

In his opinion the problem of juvenile delinquency can not be removed by legislation and it seemed probable that most of the special efforts directed against crime so over-emphasized their purposes that the subject has been kept continuously in the foreground A better method of prevention of delinquency is the quiet substitution of conditions which lead to juvenile delinquency with better environment and opportunities which will change the course of the activities of the young people and lead them to forget delinquency and crime

The author has listed some 20 traits characteristic of bad boys which must be borne in mind in any program of reform In general, the juvenile delinquents worship physical strength, desire material success, admire power and the men

who have and wield power, and they have a contempt for law and order in general They enjoy the tabloids, the sex movies, the burlesque shows, and gambling, they frequent the billiard rooms and a large proportion of them smoke and occasionally drink They are not literate, they hate effeminacy and they frequently have feelings of inferiority because of conditions at home and their lack of success in school They are usually keen in their perception and frequently size-up their teachers accurately, but appreciate sincerity, good sportsmanship and they like the teacher who gives them a "break" and when they do admire someone they are very loyal, almost blind, in their affection It is generally difficult to arouse their interest but stories of adventure and daring usually appeal to them The behavior of these young people is rarely influenced by any reference to ethical planes but if conduct is translated into terms of good sportsmanship and a consideration for others, the response is usually greater They are usually endowed with animal spirits to an excessive degree and they do not care to be watched and to be kept under supervision Any anti-crime program instituted by a community must take into consideration these inherent traits of the potential delinquent class

Prevention—Since only about ten per cent of the number of persons committing delinquencies and crimes are apprehended by the forces of law. G R Kamman^{‡1‡} has stated that more effort should be concentrated upon the prevention of juvenile delinquency than upon the multiplication of courts, prisons and methods of treatment of the criminal In reviewing the social factors linked with the production of delinquent children he has mentioned the influence of improper parental care and supervision, the poor neighborhood with its gangs

and improper employment of leisure time, the employment of children in street occupations

Considerable emphasis was placed upon the declining standards of education during the past few years, wherein the school year has been shortened in many localities and the teaching forces have been reduced by 25,000 throughout the nation while the number of school children has increased by more than a million The influence of newspapers, magazines and movies in giving information of the methods of committing crime has been great. The only way to combat such movements will be the education of public opinion against them and the assistance to schools and parents in meeting the early problems of abnormal behavior of children The provision of more healthy outlets for the child's energy in the form of sports, play facilities and the profitable use of leisure time will aid greatly in guiding the social conduct into more healthy channels

Training Juvenile Delinquents-The position of children in the community at the present day and the training of juvenile delinquents have been discussed recently by V Kersey 417 He called attention to the longer period of school attendance required and the growing demands of both industry and business for men and women with training and more extensive education There is a greater tendency now for young adults to move from place to place in seeking their education and their occupations They are demanding a chance to earn a living and to provide some security against the future Youth in general has become more health conscious, not only in protecting himself against disease and in developing physical prowess but also in desiring sports and play for recreational purposes Changes in the educational systems and in the demands of young 1066 PEDIATRICS

adults have outlined for pupils more definite objectives and plans for life work, expressions of energy and feelings of responsibility toward their communities During such periods of re-adjustment, youth frequently has difficulties in meeting new requirements and the communities fail to appreciate the changing conditions imposed upon the younger generation and consequently do not meet the demands of youth

Treatment—The organization of Coordinating Councils for the treatment and prevention of juvenile delinquency has produced successful results in California and, more recently, in other states of the union The history of this movement has been reviewed by N Fenton 416 When the problems of juvenile delinquency were beginning to be recognized, institutions were built for the care and isolation of children with social and mental diseases As this type of care became inadequate, study and treatment came to be given by the individual psychiatrist and psychologist and later by the child guidance clinic Up to the present time the efforts spent by the child guidance clinics have not reduced in any degree the incidence of juvenile delinquency It is now realized that the problem of mental hygiene belongs to the community at large

The treatment and prevention of the delinquency cover so many phases of life that only the co-ordination and co-operation of the public and private agencies of all types and the interest of the community in general can effect a reduction of juvenile delinquency Co-ordinating Councils are interested not only in the prevention of delinquency but also in the education of the public in matters of mental hygiene. The movement began in 1919 in California but it has received the greatest impetus during the past five years, when similar or-

ganizations were established in many other states and a national co-ordinating council was instituted for the purpose of giving assistance and advice to the local units

The national movement for the prevention of delinquency through community co-ordination has been reviewed by K S Beam 417 The national organization was instituted to give stability and permanence to the movement, to stimulate research and to act as a center of information and advice for the various local units The purpose of the local groups is to (a) attack the problems which are of immediate importance in their community by means of co-ordinating the activities of all types of agencies and of the trained officials who are interested in the investigation and treatment of delinquency problems, and (b) to view the work of the future which would include educational programs in college. and schools, the instruction of social workers, the solicitation of interest of the local schools, churches, clubs and juvenile courts in combating the prob-Already these councils have conducted sociological studies, helped to educate the public, encouraged the provision of recreational facilities for children, and have aided in the removal of children from poor home conditions and other unfavorable environments

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THERAPEUTICS, GENERAL

By E A DAUGHERTY, M D

ACETYLCHOLINE

Therapeutics—A C Bell and P Playfair report on the use of intramusular injections of acetylcholine in 23 cases of severe uterine inertia Only patients in whom pregnancy had been normal and in whom there was no evidence of disproportion were regarded as suitable for treatment Acetylcholine was used only after all other stimulating measures tried had failed in advancing dilatation of the cervix dose used was empirical and therefore varied The most effective method was found to be four doses of 3 grains (02 Gm) of acetylcholine given intramuscularly at intervals of three hours The full dose should be given in all cases, even though the mertia appears to have responded to treatment before the fourth dose has been given. The drug had no harmful effect on the maternal blood pressure, the fetal heart rate, the type and frequency of contractions, the dilatation of the cervix or the general effect on the patient. The maternal mortality was (one) 434 per cent and the fetal mortality was (three) 13 04 per cent (two of these fetuses were dead before acetylcholine was given)

ACRIFLAVINE

Therapeutics—Haberlin² states that in the derinatologic clinic of Zunich gonorrheal vulvovaginitis in children has been treated during the last two years by continuous irrigations with a solution of acriflavine hydrochloride, the concentration of which is gradually increased from 1 6000 to 1:2000 A Nelaton catheter, which is connected (1074)

with an irrigator, is introduced into the vagina. The catheter is fastened to the thigh. The backflow of the irrigation fluid escapes through an opening in the mattress. The treatment does not bother the child, since they can be in a half-sitting position and are able to play. The irrigation is given for approximately three hours in the morning. The drop velocity is 40 per minute. This procedure is continued for four weeks.

Of the 13 children in whom this treatment was employed, 12 remained free from relapse during observation periods of from 2 to 15 months. In one child a relapse occurred after four months, but reinfection by the mother seemed possible in this case. The author emphasizes that this method of treatment not only reduces the time required for the treatment to about half of the length formerly required but is also more effective.

ALCOHOL

Physiologic Action — L Krueger and F C MacIntosh3 reported on a series of experiments to determine the stimulating effect of alcohol in dilute solution on gastric secretion A dog equipped with a Pavlov pouch of the stomach and a gastric fistula was used in carrying out the experiments hundred cc of five per cent ethyl alcohol warmed to 98.6° F $(37^{\circ}$ C) was introduced into the stomach through the gastric fistula while the gastric glands were at rest, and the resultant pouch secretion was collected For controls two other dogs were used, one with a Heidenhain-pouch (vagal innervation destroyed) and one with a Bickelpouch (completely denervated) and gas-The Bickel-pouch dog tric fistula could be similarly given alcohol by the gastric fistula, the Heidenhainpouch dog could be given alcohol by rectum The authors observed that two or three minutes after the dilute alcohol was injected the gastric juice began to flow from the pouch The secretion was active for about an hour, and stopped after about two hours, when the main stomach was found to be empty same experiment was repeated many times over a period of several months, and it was found that the total volume, and acidity were always about the same However, a very striking observation was made in the change which occurred in the concentration of pepsin The value for pepsin after the first month or two became higher and higher The average value for pepsin concentration increased from 33 Mett units in January to 463 in September, and there was an increase in the digestive power of 1400 per cent The conclusions drawn by the authors were that with repeated alcohol injections, the dogs learned to like the alcohol, and the chemical acted as a positive conditioned stimulus for the secretion of pepsin The actual stimulus would probably be the taste of the alcohol as it was excreted in the breath This conclusion was strongly supported by experiments using the alcohol by rectum, eliminating the conditioning effect, and the digestive response of the alcohol gastric secretion was very low, although the total acidity and volume were about normal From the results obtained, the authors conclude that alcohol differs from all other chemical stimulants of gastric secretion in that it acts well from any part of the digestive tract The secretogogue action of alcohol, like histamine, is a peripheral one, since it does not require the integrity of the extrinsic innervation of the

pouch From the practical point of view, positive alimentary conditioned reflexes may easily be formed with dilute alcoholic beverages. Even in the absence of such reflexes, alcohol through its peripheral action may improve a faulty digestion by increasing the flow of juice If positive conditioned reflexes have been developed, the beneficial effect of alcohol is augmented, since the juice secreted has a greater digestive power The author suggests that if dilute alcohol is to be prescribed as an aid to gastric digestion the beverage preferred by the patient would probably possess the greatest virtue as a stomachic

ALUMINUM HYDROXIDEAND ALUMINUM SILICATE (KAOLIN)

Physiological Action—One of the oldest remedies brought down to present day medicine is kaolin (aluminur) silicate) The physiological action of kaolin in the intestinal tract is twofold

- 1 There is a mechanical action, because large numbers of bacilli are enclosed and carried off but are not killed
- 2 By adsorption the kaolin takes up

Although, kaolin has some colloidal activity the chief criterion for successful action of kaolin in a liquid medium is, that it be kept in motion, to prevent the drug from settling out and thus a large surface area for adsorptive purposes be lost Aluminum hydroxide is somewhat similar to kaolin but has a greater colloidal activity. It settles out of suspension less readily and forms a light viscid gel Under certain conditions it is capable of acting as either a weak acid or a weak base, this property alone making it useful in the treatment of peptic ulcer Because of the increased colloidal and astringent action, its value as an addition to kaolin readily becomes apparent

Therapeutics—Six cases of ulcerative colitis were treated by J B Eyerly and H C Breuhaus4 in which the aluminum hydroxide and kaolin mixture were given by rectal retention, instead of the customary oral administration One hour after the bowel has been cleansed with a pint of a warm water, a retention enema consisting of a 3 to 5 ounce (90 to 150 Gm) mixture of kaolin and aluminum hydroxide in from 3 to 5 ounces (90 to 150 cc) of warm distilled water The patient is instructed to retain this as long as there is no discomfort Normally one retention a'day is sufficient, but occasionally two are given

From the results obtained by this method of treatment Eyerly and Bleuhaus conclude that

- 1 The treatment of ulcerative colitis by aluminum hydroxide and kaolin is rational
- 2 The adsorption of bacteria and their products reduces irritation and decreases the absorption of toxins
- 3 The astringent action lessens absorption and the transudate from inflamed surfaces is diminished
- 4 It is not toxic
- 5 There is no admixture with food and digestive juices
- 6 A neutral reaction in the lumen of the bowel is preserved
- 7 No bolus or impaction formation occurs with moderate care

ARSENICALS

Toxic Effects—The literature still reports cases of toxicity resulting from the arsenicals. These vary from simple gastro-intestinal symptoms or dermatitis to severe reactions, causing jaundice, and blood dyscrasias. The nature of the drugs being better understood today however, makes prophylaxis and treatment easier than it was in the past

F. E. Cormia⁵ thought from previous experimental work that some unknown factor was responsible for cutaneous idiosyncrasy to neoarsphenamine. Further investigations, according to the author, indicate a distinct relationship with Vitamin C. Experiments on animals suggest that a diet rich in Vitamin C should be of value to patients receiving an arsphenamine, and particularly to those who had inadvertently received a paravenous injection. Intensive therapy with ascorbic acid, may be of value in cases of post-arsphenamine dermatitis.

C C Dennie and E S Miller⁶ report on two cases of arsenical dermatitis followed by paralytic ileus, perforation of the intestine, and death. The toxic action appears to have been due to the corrosive action of arsenic on the intestinal mucosa

F E Cormia⁷ reports a fatal case of hemorrhagic encephalitis following the use of arsphenamines in a young pregnant woman with latent syphilis Unusual widespread vascular paralysis developed, and was thought to be due to overdosage. The author suggests that the maximum dose of neoarsphenamine in pregnancy should be 0.3 Gm weekly. Cormia believes that this type of complication is more common in pregnant women. Adrenalin in large doses and spinal dramage should be used if signs of cerebral edema appear.

A E W McLachlan⁸ reports on 14 cases of dermatitis, one of purpura, and three of jaundice, resulting from arsphenamine and bismuth therapy. The author recommends intravenous calcium thiosulfate as a remedy for these complications. The above cases all cleared up promptly with the treatment suggested. The dose is 0.45 to 0.9 Gm in ten per cent solution injected intravenously.

T Weinberg⁹ reports on three cases of shock following intravenous therapy with neoarsphenamine All three patients presented a typical picture of shock The first two patients remained in shock for about six hours each, while the third patient maintained this state for about six days None of the three patients responded to epinephrine or similar stimulants, but they did respond well to the usual shock therapy Patients one and three received intravenous fluids, and patient two received heat to the extremities and oxygen All three patients had persistent vomiting and cold sweats with cold clanmy skins The author suggests that arsenoxide plays a part in this toxic manifestation, but in addition there appears to be an x factor not yet discovered

Arsenoxide (Mapharsen)

Therapeutics—R P Parsons¹⁰ discusses the use of arsenoxide in the treatment of 25 cases of early syphilis Alternate courses of bismuth compounds were also administered. The cases have been under treatment and observation from 10 to 23 months, the average being 16 months Prior antisyphilitic treatment had not been administered in any of the cases The age of the infections averaged 17 days (from the appearance of primary lesion to beginning of treatment) Twenty of the cases had positive darkfields, and of these, 15 had positive Kahn tests before treatment was started The darkfields became negative in from one to five days after the first injection, the average was 15 days Among the 21 positive Kahn cases, 20 became negative after from 4 to 20 injections, the average was 89 injections. The other case remained four plus until 20 injections each of arsenoxide and a bismuth compound had been given and then remained two plus until 30 injections of arsenoxide had been given. The Kahn test has since remained negative. No instance of clinical and only one of sero-logic relapse has been observed. Spinal fluid examinations in 19 of 22 cases (treated for one year) were found negative in all phases. Only very mild forms of reactions were seen. Mild Herxheimer reactions were observed following the initial dose in two secondary cases and one late primary case. Further use of the drug produced no subsequent reactions in any of these three cases.

Pharmacology-L M Wieder, O H Foerster and H R. Foerster¹¹ in a brief discussion concerning the pharmacology of arsenoxide state that it is a drug of definite constitution (the hemialcocholate of three-amino-four-hydroxyphenylarsine oxide hydrochloride). and is assayable by chemical instead of biologic methods, hence it may be expected to be of uniform potency chemical constitution indicates that it is without the power to produce nitritoid shock, and this supposition has been in accord with the clinical experience of the authors The drug becomes less toxic and only slowly less potent on prolonged exposure to the air and therefore may be prepared well in advance of the time of injection without risk of danger of therapeutic failure The arsenical content of arsenoxide is approximately the same as that of the arsphenamines, and as the effective therapeutic dose is much smaller, less arsenic is introduced

Technic of Administration—The preparation for injection and the method of administration are exactly the same as those used for neoarsphenamine except that when arsenoxide is used the drug should be injected into the vein rapidly. Pain along the course of the vein and in the shoulder immediately after injection has been reported by

many investigators Rapid injection of the drug in the author's experience failed to produce this reaction A solution containing 4 mg. of arsenoxide per cubic centimeter of distilled water is isotonic Arsenoxide is freely soluble, requires no neutralization and acquires a light brownish color on prolonged standing. Discoloration of this nature seems to be no contraindication to its use

Toxic Reactions-Toxic reactions to arsenoxide are discussed by H N Cole and R B Palmer¹² in their study of the effect of the drug on 242 patients with syphilis The study extended over a period of three years. The patients received 5030 injections, with a total of 269,790 mg of the drug Therapy consisted of alternate courses of arsenoxide and a bismuth preparation Observations were made on the Herxheimer reaction, or therapeutic shock, and on toxic manifestations, both immediate and delayed The authors state in conclusion, that the Herxheimer reaction in both the focal and the systemic phase, is promment With an initial dose of 30 or 40 mg this reaction was frequently severe The immediate toxic reactions of a mild degree were chiefly gastrointestinal in nature Of the 167 patients experiencing mild reactions, 93 or 52 69 per cent, had minor gastro-intestinal reactions (nausea, emesis, or diarrhea, or all three) on two or more occasions. In this series of 242 patients, 15 patients had immediate toxic reactions that were more severe Concerning delayed toxic reactions, there were no instances of encephalitis, neuritis, or involvement of the hematopoietic system There was one case of laundice in which arsenoxide seemed to be the only causative factor Pain in the arm along the course of the vein occurred after 89 injections Slight perivascular leakage occurred after 18 injections, with the local inflammatory reaction and pain subsiding rapidly Nodular infiltration, formation of abscesses, necrosis and sloughs were not observed in any case

BARBITURIC ACID AND ITS DERIVATIVES

Addiction—G W Robinson, Jr., 13 discusses some of the ill effects of the derivatives of barbituric acid The little experimental work that has been done on heavy doses shows definite changes in the brain The barbiturates fall into the group of addiction-producing drugs This statement is corroborated by the report of four cases in which the barbiturates were habit forming in certain psychologic types This addictive action is similar to that of alcohol There 1s, of course, a strong psychogenic factor in this class of cases, but the psychogenic factors are important in all forms of addiction requires a certain personality pattern in order that addiction may develop Excessive doses destroy cerebral tissue and produce extreme toxicity Barbital addicts will take excessive doses and the deterioration frequently seen in these cases is due to destruction of cerebral tissue, which is accumulative over a period of time to a great enough extent to interfere with the patient's efficiency The development of tolerance, while not as marked with these drugs as with some other forms of addiction-producing drugs, nevertheless leads the barbital addict into taking larger and larger doses so that the patient is soon taking toxic doses, which not only produce the clinical evidence of toxicity but also produce pathologic changes in the brain These acute changes probably are the cause of the neurologic symptoms seen in barbital poisoning, both fatal and nonfatal Laymen will use barbital as the addict to alcohol uses alcohol

BENZEDRINE SULFATE (Beta-Phenylisopropylamine)

Physiological Action-In studying the effects of benzedrine sulfate on a group of normal persons and a group of depressed patients, E Davidoff and E C Reifenstein¹⁴ observed that the drug had a definite stimulating effect on the central nervous system Following the administration of the drug there was (1) Elevation of mood, (2) talkativeness, (3) increased motor activity, and (4) improvement in general efficiency Other effects observed were insomnia and decrease in sleep require-In general the most marked response in all the various phases studied was found in the normal group The organic cases, particularly the alcoholic and post-traumatic closely paralleled the normal, while the psychogenic group showed the least response

The authors also studied the peripheral effects of the drug observed in the various groups The most prominent changes noted were, flushing of the face, urticaria, generalized sensation of warmth, sweating, coldness and clamminess of the hands, greasiness of the skin, sensations of constriction, fulness or aching of the head, increase or decrease in nasal secretions, dilatation of pupils, and dryness of mouth and throat Body weight decreased in most subjects Blood pressure and pulse were variable, some showing an increase while others were decreased Respirations were apparently not affected The temperature was variable, as was the basal metabolic rate There was no striking variation in the blood

Indications — Benzedrine sulfate has been widely accepted as a local astringent. As an internal medication it has been best established in the treatment of narcolepsy. It has been suggested in

overcoming persistent states of fatigue and "nervous exhaustion," and in post-encephalitic parkinsonism. Also, in relieving gastro-intestinal spasm, in combating overdoses of barbiturates. The author believes many of the above suggestions need further experimental evidence and clinical proof to substantiate the use of the drug.

Contraindications—It is generally agreed by all investigators that the presence of (a) hypertension, (b) coronary artery disease, and (c) a state of manic excitement are definite contraindications to the use of the drug In addition to the above Davidoff and Reifenstein consider that there are a number of circumstances, such as (idiosyncrasy to small doses, severe forms of vasomotor instability, wide daily fluctuations in blood pressure or pulse rate, history of convulsive seizures, the presence of anorexia, insomnia and lowered bodily resistance), in which the drug should be used with great caution.

Dosage—In view of the disturbing nature of some of the untoward reactions, it is always advisable to start administering benzedrine in small doses Davidoff and Reifenstein state that most of their patients received ½ to ½ grain (10 to 30 mg) of the drug daily. Some of the unresponsive patients appeared equally unaffected with doses of from ½ to ½ grains (20 to 70 mg). In those individuals showing a response to the drug, the reaction appeared from one to three hours after administration and persisted from three to eight or nine hours

Therapeutics—The effect of benzedrine was studied by P Solomon, R S
Mitchell and M Prinzmetal¹⁵ in 28
patients with postencephalitic Parkinson's disease The dose varied from
½ to 2½ grains (10 to 160 mg) orally
per day, either alone or in combination
with scopolamine, or stromonium

They found from their observations that benzedrine sulfate is useful in the symptomatic treatment of postencephalitic Parkinson's disease Used alone, benzedrine is effective in this condition when the symptoms of drowsiness and lack of energy predominate, but usually it is most effective when used in combination with scopolamine or stromonium authors found that subjective improvement in muscular rigidity and strength was noted in 70 per cent of the cases Benzedrine seems to act specifically in abolishing or reducing the number and severity of oculogyric crises The drug was found to be of no value in ten cases of arteriosclerotic Parkinson's disease The authors conclude that benzedrine has a greater stimulating action on the central nervous system than ephedrine and the drug should be used cautiously until more is known about it

I Finkelman and L B Shapiro 16 treated 12 patients with postencephalitic parkinsonism during consecutive periods with atropine, benzedrine sulfate plus atropine, benzedrine sulfate alone, and again with benzedrine sulfate plus atro-The dose of benzedrine sulfate ranging from 13 to 12 grain (20 to 30 mg) a day, one half of the dose being given at 7 v M and the other haf at noon. The best results, according to the authors, were obtained during the combined treatment of atropine and benzedrine sulfate Although atropine alone caused a diminution of tremor and rigidity, the addition of benzedrine sulfate caused improvement in the sleep cycle and reduced the frequency or caused the disappearance of oculogyric crises, and there was a feeling of increased energy

H Ulrich¹⁷ reports on the use of benzedrine sulfate in the treatment of ten cases of narcolepsy, and concludes that oral medication with the drug appears to be the only satisfactory method of

treatment Several cases of long-continued use of the drug are reported and no permanent deleterious effects were noted, and there was no evidence of habit formation.

CALCIUM

Physiologic Factors — To understand the proper use of calcium in medication, it is essential to appreciate the exchange of calcium in the normal body Calcium is not only stored in the soft tissues of the body, but also in large quantities in the bones

After absorption from the intestine, calcium may be promptly excreted or may be deposited, and excreted calcium may come from the blood, or from this reservoir in the bones. Partly as a result of this reserve, the calcium levels in the blood stream remain fairly constant in health and in most diseases.

Also, abnormal calcium metabolism is so often related to or influenced by the internal secretions and vitamins that adequate calcium therapy canot be given without their adjustment and regulation

The factors that may influence either the calcium storage or blood levels are discussed by J C Aub 18 The author states that diets inadequate in either calcium or phosphorus, especially acid ash diets the body storehouse of calcium would be depleted, without any necessary depletion in the blood level Excessive amount of both thyroid and anterior pituitary secretion stimulate the calcium excretion to abnormally high levels In hypothyroidism the calcium excretion is below normal The secretion of the parathyroid glands has no influence on calcium absorption from the intestines, but markedly influences the calcium and phosphorus levels in the blood stream. Deficient secretion is associated with a lower blood calcium and an elevated blood phosphorus and a diminished excretion of both in the urine

Excessive secretion raises the blood calcium, lowers the blood phosphorus and is associated with increased excretion of both in the urine

Therapeutic doses of vitamin D greatly facilitates absorption of calcium from the intestine and also the deposit of calcium phosphate in the bones. In excessive doses its action is almost identical with that of parathyroid extract on the blood and excretion levels. In vitamin D deficiencies you get the picture of infantile or adult rickets with normal blood calcium and lowered blood phosphorus.

Vitamin C (cevitaminic acid) causes a rapid deposit of calcium at the epiphysial ends of bones and in trabeculae

Steatorrhea, or Gie's disease, prevents the absorption of calcium because insoluble calcium soaps are formed in the intestine. Any tumor that has multiple metastases in bone may apparently cause an elevation of blood calcium with a normal blood phosphorus level.

Severe chronic nephritis according to the author may also cause abnormalities in the blood with a low blood calcium, and a high blood phosphorus level

Therapeutics—The intelligent use of calcium depends on a knowledge of the abnormality involved in its complicated metabolism. The success of therapy rests in the correction of the fundamental abnormality.

Increased ingestion of calcium, Aub states, is necessary in all cases where there is depletion of the calcium stores in the bones, no matter what the cause This is best accomplished by the drinking of large quantities of milk, because calcium in this food is readily absorbable Calcium gluconate and calcium lactate may be used where milk is not tolerated. Calcium gluconate requires 172 grains (11.2 Gm.) and calcium lac-

tate 120 grains (77 Gm) to include 15 grains (1 Gm) of calcium a day Normally 05 to 1 Gm of calcium is an adequate daily intake and two Gm. is considered a high daily intake, by the author When absorption of large quantities of calcium is desired, the vitamin D intake should be adequately maintained.

In severe tetany associated with a low blood calcium, the need for calcium therapy may be so great that its intravenous use is essential. Under these conditions two salts of calcium may be utilized. Sterile calcium chloride may be given intravenously in doses of 10 cc of a five per cent solution. It has several disadvantages, for occasionally thrombosis of the vein may follow its use, and if any of it is injected in the extravascular spaces a slough is apt to result.

The author recommends calcium gluconate, therefore, because it may be given without these disadvantages and may be given intramuscularly. In doses of 10 cc of a 20 per cent solution it produces the characteristic calcium effect

Calcium gluconate is of value also in other spasms of smooth muscle It has a very beneficial effect in acute lead colic, in which morphia and other sedatives are not very efficient. The author states intravenous administration of calcium compounds is of value in the treatment of acute gallstone colic and renal colic The intramuscular use of the calcium salt appears to be indicated only in order to prolong the effects of intravenous therapy, or for more rapid absorption than can be obtained through the gastrointestinal tract Calcium chloride should never be so used for intramuscular injection because of its necrosing effect on the tissues Calcium compounds by mouth are limited to more chronic conditions in which there is no urgency with regard to calcium absorption. A high calcium diet can easily be obtained by means of milk, eggs, and green vegetables. If calcium salts need to be added, they are most easily taken as calcium carbonate or calcium gluconate or lactate, in a dose up to 154 to 231 grains (10 to 15 Gm.) per day. Adequate doses of vitamin D should always be given to facilitate the absorption of calcium through the intestinal mucosa.

A high calcium intake is desirable during pregnancy, especially during the latter half, in order to prepare for the drain on the calcium storage which occurs during lactation. A daily intake of 30 grains (2 Gm.) of calcium should be provided, to insure a positive calcium balance. From the observations of Ann Minot high calcium intake is of great therapeutic value in acute liver damage. This was particularly true in the liver damage following carbon tetrachloride poisoning in animals.

High calcium intake is made use of by dermatologists in eczema and similar conditions, and also in the treatment of allergic diseases, although the physiologic indication is not absolutely clear

CALCIUM CHLORIDE

Therapeutics—E Muff¹⁹ reports on the use of calcium chloride for the prevention of fatal postoperative pulmonary embolisms. The author states that the use of calcium chloride for this purpose was first introduced in Bier's Clinic. The technic of this method calls for the daily subcutaneous injection of 1 cc of a 0.01 per cent solution of calcium chloride intramuscularly into the thigh or the gluteal muscle. According to Martin's directions, (who reported on the prophylaxis in Bier's clinic) the injections as given daily for eight successive days after operations or injuries. If

signs of thrombosis or if pulmonary infarct appear, the injections are continued for two weeks. The author does not claim that calcium prophylaxis alone will prevent every fatal embolism. However, since the embolus usually originates in a symptomless distant thrombosis, the author believes that a measure which increases the adhesiveness of such thrombi appears valuable

CARDIAZOL

(Pentamethylentetrazol), (Metrazol)

Therapeutics—L A Finiefs²⁰ reports the use of *cardiazol* in artificial convulsive seizures in patients suffering from schizophrenia. It has been known for sometime that many patients suffering from schizophrenia, were prone to have remissions, or be much improved following an epileptic seizure. It was with this in mind that psychiatrists have been attempting by the use of drugs to evolve a form of treatment by inducing fits artificially

Technic - Finiefs uses the following technic in producing the convulsive seizure All previous medication, especially of sedatives should be discontinued for a few days beforehand Cardiazol is supplied in ampules of 11 cc solution, each containing 01 Gm of cardiazol in 1 cc It is injected, intravenously once or twice a week, with at least two clear days between each injection The patient, having had an enema the previous evening and no morning meal, is kept in bed and injected at 8 The initial dose should be 05 Gm of cardiazol, and if this dose does not produce a fit, it should be increased at the following injection by 0.1 Gm until the fit producing dose is reached This dose is then repeated at subsequent injections The highest dose reported is 1 Gm The fit occurs one-half to one minute after the injection, lasts for about two minutes, and has all the dramatic appearance of a grand mal attack. The patient remains dazed afterwards for a short time and restlessness may follow, but this is temporary and should not be controlled by sedatives.

More often the patient falls asleep, and he should remain in bed for the rest of the day Food should not be given for four to five hours after the fit as there is danger of vomiting. No other complications have been met with. The number of fits required varies considerably, the average being about 30. Remissions have been obtained according to Finiefs with as few as four, but in general if no mental change is noticed after 20 fits the treatment is stopped.

Contraindications—The treatment is contraindicated in all febrile conditions, and pulmonary, cardiovascular, and renal disease are absolute contraindications

The author concludes, that although no improving figures of recoveries can as yet be produced, the treatment has been used at the Three Counties Hospital for several months, with fairly good results. The treatment is very active and somewhat rough, but no ill effects have been observed in carefully selected healthy young patients. The method appears especially beneficial in early psychoses especially the stupoiose and catatonic

G W B James, R Freudenberg and A T Cannon²¹ report that they have induced occasional epileptiform fits by injecting cardiazol into some of their patients undergoing high-dosage insulin treatment on days when insulin is omitted, for the cardiazol fits are less dangerous than those of hypoglycemia and may be used as a supplement

DIETHYLENE GLYCOL

Poisoning—The recent investigation carried out under the auspices of the A M A Chemical Laboratory²² decided definitely that diethylene glycol when taken internally in sufficient quantity, and in divided doses is a decidedly toxic substance and cumulative poison preliminary report of toxicity studies by E. M. K. Geiling, J. M. Coon and E. W. Schoeffel²³ on rats, rabbits, and dogs showed that all the rats receiving doses of two cc or more of diethylene glycol died in from two to five days with terminal anuria The clinical picture as seen in rats was as follows Increased thirst, and diuresis, food is refused, later urine excretion becomes scanty, finally respirations increase in rapidity and depth and anuria sets in, followed by coma and death Rabbits react in essentially the same manner Dogs, also, behave in the same manner, but the dose is hard to determine because the animals vomit after the drug is administered The necropsies of four patients following the administration of a proprietary preparation of elixir sulfanilamide, in which the diethylene glycol was found to be the toxic agent causing death are reported on by O E Hagebusch 24 The four autopsies revealed essentially the same findings, pulmonary edema, marked nephritis, with hemorrhage into the cortex of the kidney, marked hemorrhage in the pericardium, mucosa of the stomach and duodenum and into serous surfaces of lung and liver From the report of P R Cannon25 the pathologic effects are essentially the same in dogs, rats, and rabbits following the ingestion of the drug The general picture Cannon states, is that of a severe chemical nephrosis with intracellular edema of most of the epithelial cells of the convoluted tubules, resulting in tubular obstruction by compression and by the intraluminal formation of casts

Treatment—In regard to treatment due to diethylene glycol poisoning the A M A Chemical Laboratory reports so far as has been determined, there is no known antidote for diethylene glyco poisoning, when taken internally in lethal doses Gastric lavage, calcium therapy orally or intravenously and 50 per cent dextrose solution intravenously with or without sodium bicarbonate have been suggested

DINITROPHENOL

Toxicity—S Simkins²⁶ reports the use of therapeutic doses of dinitrophenol alone, or in combination with desiccated thyroid, in 159 obese patients. According to the author dinitrophenol in therapeutic doses is apparently non-toxic to the liver, kidneys, and heart Neutropenias are rare Peripheral neuritis is rather common, but not troublesome The most common toxic action observed in the use of the drug was skin rashes One of the more recent toxic problems complicating dinitrophenol therapy discussed by Simkins is the development of cataracts. It has only been slightly more than a year ago that the first reports erept into the literature and since that time numerous cases have been reported The shortest time reported for the development of cataracts is one month, the longest 24 months. The number of cases reported according to the author ranges between 50 and 100. An interesting feature disclosed by studying the reported cases, is the fact that dimness of vision was usually associated with patients who had more than one course of dinitrophenol Many authors deny the role of dinitrophenol as the causative agent of these cataracts However, the author concludes that the indiscriminate clinical use of dinitrophenol should be discontinued until the vexing problem of cataracts complicating dinitrophenol therapy is solved

ETHER

Therapeutics—N L Bloise and E. A Perez²⁷ advise the use of daily ether enemas in the treatment of whooping cough The formula consists of 20 cc of a ten per cent solution of camphor in ether, 30 Gm of eucalyptol and 100 cc of a four per cent solution of aromatized oil in liquid petrolatum. The enema is given through a No 14 or 16 Nelaton catheter introduced 15 cm into the rectum The dose for each enema is five co for infants. 10 cc for children from two to eight years of age and 15 cc for older children The treatment consists of eight enemas (one a day) and in severe cases. The authors conclude that the ether enemas favorably modify the evolution of whooping cough and prevent the development of complications, especially of the respiratory tract. The number of attacks and duration of the disease are greatly reduced. The technic is simple and may be carried out by the mother at home Infants and children have complete tolerance to the treatment, which can be given with specific vaccines (freshly prepared) or with antispasmodic drugs, such as belladonna The author reports satisfactory results from the treatment in 80 per cent of a group of 80 children treated

FISH LIVER OILS

Experimental — The great therapeutic value of the fish liver oils lies not in their fat content, but rather in their high content of vitamins A and D

Until recently it was generally assumed that the vitamin D of fish oils is a single substance. Its concentration was

known to vary widely in the liver oils of different species, or even in a particular species, but that the vitamin varies in kind, as well as in amount, was not appreciated before the investigation of tuna liver oil by C E Bills, O N Massengale and M Imboden ²⁸

The Journal of Nutrition29 contains a report by the above authors, in which the liver oils of 25 species of fish were assayed in comparison with cod liver oil on rats In comparing rat unit and chickens for rat unit some of the oils resembled cod liver oil, several were definitely less effective, and a few were more The authors explain their findings on the basis that two (or more than two) kinds of vitamin D exist in fish oils and they believe that it now seems unlikely that any particular fish oil, such as cod liver oil, contains one kind exclusively The oils that proved to be the least effective were those from the bluefin tuna of California, oriental tuna, striped tuna, bonito albacore and totuava The relatively most effective oil was that from the white sea-bass of California The authors also mention that from their results it is obvious that there is no relation between the vitamin A content of the oils and the efficiency ratio of their vitamin D

R W Haman and H Steenbock ³⁰ in studying the antirachitic effectiveness of vitamin D from various sources found that in regard to the various fish oils studied, viz, cod liver oil, halibut liver oil, tuna liver oil, burbot oil and sardine oil, the comparative antirachitic effectiveness of the oils was approximately the same However, the commercial tuna liver oil that was fed was somewhat less effective than the other oils used

Cod Liver Oil

The chief fish liver oil used therapeutically and the only official one (according to the U. S. Pharmacopeia XI) is cod liver oil It is the partially destearmated fixed oil obtained from fresh livers of Gadus Morrhua, and of other species of the family Gadidae, (haddock, hake, ling and pollock).

Therapeutics—1. Cod liver oil is now widely used as an adjunct in infant feeding. The oil is rich in both vitamins A and D and contains a readily digested fat.

- 2 It has a wide field of usefulness in women during pregnancy and during the period of lactation
- 3 The oil has a favorable influence in conditions resulting from calcium and phosphorus imbalance
- 4 In tooth caries in conjunction with vitamin C
- 5 As an application to infected wounds and burns

Potency and Dosage-The U S Pharmacopeia specifies that cod liver oil must contain in each gram at least 600 U S. P. units of vitamin A and at least 85 USP units of vitamin D, and further provides that the vitamin A potency and vitamin D potency of cod liver oil when designated shall be expressed in "United States Pharmacopeia units" per grain of oil and may be referred to as "U S P units" per gram of oil Cod liver oil may be flavored by the addition of not more than one per cent of any one or any mixture of flavoring substances recognized in this pharmacopeia

The U S P XI average dose of cod liver oil for an infant is 1 fluid dram (4 cc) and the adult dose is 2 fluid drams (8 cc) three times daily

Fish Liver Oil Preparations (N.N.R.)

Cod liver oil, because of its abundance and regularity of its supply, is the liver oil most extensively used in medicine today, however, there are several other fish liver oils that are a potent source of vitamins A and D, and, while they are not included in the present Pharmacopeia, they stand accepted by the Council on Pharmacy and Chemistry of the American Medical Association on January 1, 1937

Halibut Liver Oil—Oleum Hippoglossi—A fixed oil obtained from the fresh livers of Hippoglossus hippoglossus It is biologically assayed to have a potency of not less than 44,800 units of vitamin A (USP) per gram and not less than 540 units of vitamin D (USP) per gram

Halibut liver oil is a yellow to brownish yellow, oily liquid, having a slightly fish odor and taste. Its uses are the same as for cod liver oil

Dosage—For infants 6 to 10 drops (25 to 35 minims) daily, for premature and rapidly growing infants, 15 drops (525 minims) daily. For severe vitamin deficiencies, 20 drops (7 minims) or more may be given daily.

Percomorph Liver Oil—Oleum Percomorphum—A mixture containing the fixed oils obtained from the fresh livers of the percomorph fishes, containing 50 per cent of cod liver oil It is a yellow to brownish yellow, oily liquid, with a slightly fishy but not rancid odor and a fishy taste Percomorph liver oil is biologically assayed to have a potency of not less than 60,000 units of vitamin A (USP) per gram and not less than 8500 units of vitamin I) (USP) per gram Its uses are the same as those for cod liver oil

Dosage—Prophylactic, for normal infants 10 drops daily, curative and in severe conditions, up to 20 drops daily

Burbot Liver Oil—The oil extracted from the livers of the Burbot (Lota maculosa) family Gadidae Burbot liver

oil is a pale yellow, oily liquid. It has a slightly fishy but not rancid odor and a fishy taste. Burbot liver oil is biologically assayed to have a potency of not less than 4480 units of vitamin A (USP) per gram and of not less than 640 units of vitamin D (USP) per gram. The uses are the same as those of cod liver oil.

Dosage — Prophylactic, 16 minims (1 cc) daily As a curative dose and in severe conditions the amount should be increased depending on the severity of the condition

GOLD

Therapeutics — C E H Ason,31 in a general survey of the use of gold salts in the treatment of pulmonary tuberculosis, remarks that gold therapy is of real value in (1) recent acute spread or exacerbation of exudative disease in a bilateral case, (2) acute spread of disease in a fibroid case, (3) some cases of bilateral disease, combined with collapse therapy In cases with persistent tubercle bacıllı in the sputum and in cases becoming gradually worse under other treatment it may be given with varying success It is contraindicated in the presence of intestinal or renal tuberculosis or of persistent albuminuria, in cases with high fever, and in those showing rapid softening of the lung tissue with advancing excavation

The form in which gold is generally used is the double thiosulfate of gold and sodium. The dose is progressive, commencing with 0.01 Gm and rising by degrees to 1.0 Gm. It is given intravenously, the required dose being dissolved in from 5 to 20 cc of double-distilled water and the strength of the solution should never exceed five per cent.

From a study of 60 selected cases treated with various gold salts, J. C. Banerjea³² finds that about one-half of the cases with recent exudative lesions were definitely improved. This form of treatment must be regarded, as an aid to the conservative treatment of rest, nutritious diet and fresh air

W S C Copeman and W. Tegner³³ report the use of gold therapy in a series of 51 cases of rheumatoid arthritis Great improvement or recovery was noted in 58 per cent. Improvement was usually preceded by a fall in the sedimentation rate. This being an important point in prognosis. The authors conclude that gold is the medicament of choice in early cases of the rheumatoid arthritic type when the sedimentation rate is raised.

Untoward Effects — Copeman and Tegner in their series of 51 cases of *iheumatoid arthritis*, encountered untoward effects in 12 cases, only three of which were severe enough to necessitate discontinuance of treatment. The toxic manifestations were persistent exfoliative derinatitis, rectal spasin, hemorrhage and stomatitis.

HISTAMINE

Therapeutics — L Perlès reports34 on the use of histamine bichlorhydrate in the treatment of rheumatism cording to the author's method a solution of histamine bichlorhydrate in the strength of 0.5 mgm per cubic centimeter is employed, to which is added a small dose of local anesthetic syringe is used calibrated in 005 cc, he then injects intradermally a series of minute doses, over an area where the patient indicates that he has pain Each injection is about $\frac{1}{80}$ to $\frac{1}{10}$ of a cubic centimeter and separated by at least 1 cm Injections must be made rapidly and not more than 1/4 to 1/2 mgm of the histamine should be used in all at each treatment. At the beginning the first three or four series of injections are made daily and later every second day. The total number of injections depends upon the results, but if no benefit is obtained after ten sessions, the treatment should be discontinued. It is claimed that the treatment not only has a beneficial effect on the pain, but also upon the general rheumatic condition. The method is contraindicated in infectious rheumatism in the acute or subacute stage

E Aron³⁵ discusses the use of histamine and histidine combined in the treatment of rheumatic disorders Aron reveals three points of prime importance concerning the action of intradermal injections First, the intradermal injection of all substances at the painful area has an analgesic action Second, the intradermal route augments the rapidity and the efficacy of the action of the neurotropic substances (histidine) Third, the intradermal injection of histamine by its special vasodilator effect and by its general action is an efficacious method in the treatment of the pain and the contracture of rheumatic disorders author employs a histidine solution of four parts in 100, which contained 0.1 mg of histamine per cubic centimeter. A 1 cc. syringe and needles used for subcutaneous injection are sufficient. Never more than 1 cc of the solution was injected at one time and rarely more than one or two injections at each session. The patient himself usually indicated the painful areas of the skin The total number of injections was from six to twelve. One injection was given daily or every other day. The results so far obtained with the method have been encouraging and further study on larger groups will be necessary to give a definite evaluation of the method

HISTIDINE

Therapeutics — R Upham and H Barowsky³⁶ report on 50 patients studied to determine the efficacy of *histidine* hydrochloride as a therapeutic agent in the treatment of peptic ulcer. The group consisted entirely of men between the ages of 22 and 52 years and all were ambulatory. Only patients with duodenal ulcer were selected and an x-ray examination all showed the characteristic "duodenal cap deformity"

Method—Twenty-five of the patients received daily intramuscular injections of 5 cc of histidine solution and the other 25 received sterile water injections. At the beginning all other therapeutic factors, such as diet and the administration of alkalis and antispasmodics, were eliminated. The patients remained on a liberal diet. If at the end of the first week marked relief was not obtained, they were advised to stay on a modified Sippy diet. At the end of the second week, if they still complained of symptoms, antacids and antispasmodics were added

Results—Only one patient out of the 25 studied was relieved completely by the histidine injections. Twenty-four patients had definite symptoms at the end of the first week and were put on a modified Sippy diet. In this group, 13 obtained from marked to complete relief within 24 to 48 hours. At the end of the second week antispasmodics and antacids were administered to the remaining 11. Only three obtained relief. The remaining eight patients obtained no relief throughout the course of the treatment.

Of the remaining 25 patients treated with sterile water, three obtained complete relief of symptoms despite the fact they were on a liberal diet. At the end of the first week, the remaining 22 were

placed on a modified Sippy diet, with 14 obtaining from marked to complete relief of symptoms in from 24 to 48 hours Two others were definitely relieved of symptoms on the addition of antacid and antispasmodics, at the end of the second week Six patients failed to respond to any form of treatment With this graduated form of therapy, the majority of the patients studied obtained definite relief only when a modified Sippy treatment was instituted, also the injection of sterile water resulted in slightly more so-called cures than the histidine form of therapy From these results, the authors conclude, that histidine not only lacks specificity but is no more beneficial than the injection of sterile water in the therapy of peptic ulcer

IRON

Therapeutics—The use of iron in the treatment of hypochromic anemias is discussed by C. C. Ungley 37. The author believes iron is the essential therapeutic agent for hypochronic anemia whether this is caused by dietary deficiency, achlorhydria or other gastrointestinal defect, chronic blood loss or pregnancy When the anemia is hypochronic and associated with an iron deficiency, the daily administration of sufficient amounts of iron usually gives rise to a reticulocyte response the height of which is in general proportional to the initial level of red blood cells and hemoglobin from the improvement in the red blood cell count and hemoglobin, iron therapy results in improved appetite, gain in weight and frequently a diminution of digestive disturbances Iron in large doses is rarely constipating, a laxative effect may be noted in some cases especially early in the treatment. The author states that iron acts almost as a specific in arresting juvenile menorrhagia, nose bleeding and other manifestation of a hemorrhagic tendency. Inorganic iron by mouth is the drug of choice in hypochromic anemias. The author deplores the use of infinitesimal quantities of iron by injection or the use of the relatively ineffective organic combinations of iron

Dosage—Inorganic iron may be given either as reduced iron, as ferrous salts (sulfate, chloride, lactate), or as ferric salts (ferric ammonium citrate or ferric chloride) Ferrous salts are effective in smaller doses than ferric salts average daily doses which are necessary to secure maximal effects, are given by the author as ferric ammonium citrate 90 grains (6 Gm), ferrous carbonate (Blaud's pill) 60 grains (4 Gm), reduced iron 45 grains (3 Gm), ferrous sulfate 12 grains (08 Gm) If causes for iron deficiency persist or if no facilities for regular blood counts are available, iron therapy should be continued indefinitely, usually, however, at about one-third to one-half the dosage mentioned above Iron needs no supplement in the majority of cases a well-balanced diet adequate in meat, green vegetables and fruits will usually suffice Copper is present in sufficient quantities in an ordinary mixed diet and as an impurity in iron preparations but it may sometimes be of value in hypochronic anemias of infants

LIVER

Therapeutics—The use of liver and liver extracts in the treatment of pernicious and related macrocytic anemias is discussed by C C Ungley 35 In the use of liver by mouth good results can be obtained, provided the intake of potent material is adequate. However, very frequently especially, if the anemia is severe, the amount of material required is more than the patient can tolerate. This frequently occurs with cooked or

raw liver To use adequate treatment with oral liver extract entails considerable expense and also underdosage often results from failing to realize that the extract has considerably less potency than the amount of liver from which it was derived

The above disadvantages of oral treatment can be almost completely overcome by the use of parenteral liver therapy and should be the method of choice in giving liver extract. Deficient intake due to nausea and vomiting and distaste for the materials are overcome and variations in effect due to absorption from the alimentary tract are eliminated.

In severely anemic patients the response to parenteral liver therapy is decidedly more striking and more certain than with oral administration The dosage depends on the individual needs, severe cases requiring 30 to 60 units of an effective liver extract injected intramuscularly either at once or in divided doses over a period of two or three days The author defines a "unit" as the daily dose of the particular extract being used In the average patient ten units will usually cause rapid improvement and an increase of red blood cells and hemoglobin, however, certain inhibitory factors such as infection, arteriosclerosis and nitrogen retention cannot always be excluded, therefore, adequate dosage is always the better policy. In less severely anemic patients an initial injection of 20 units, followed by ten units every seven days is usually sufficient. Liver extract should be injected intramuscularly into the upper and outer quadrant of the buttock, avoiding veins. Ten unit doses per week are continued until the red blood cells are normal in all respects, with a color index of one or less and a cell size below 100 When there are no minor cubic micra neural symptoms, then ten units approximately every two weeks are sufficient. To avoid relapses and the risk of spinal cord degeneration the author believes it advisable to continue permanently and without interruption to give doses of potent material in excess of the amounts required to maintain a normal blood picture.

MAGNESIUM TRISILICATE

Physiological Properties—The application of magnesium trisilicate in the treatment of gastrointestinal disease, particularly peptic ulcer, represents a new use for a chemical compound of this type. Only recently has attention been directed toward improving ulcer therapy by development of compounds which adsorb and inactivate hydrochloric acid, in preference to those which act by direct chemical neutralization.

The recent work of N Mutch³⁸ has demonstrated that magnesium trisilicate has many advantages in this type of treatment and is able, in very small doses, to inactivate quantities of hydrochloric acid formerly requiring considerable volumes of alkali for neutralization. The results of the experimental work of the author showed that magnesium trisilicate had the following physiological properties that made it particularly applicable in treating ulcer cases

- I It differs from all other antacids in clinical use in the vigor of its adsorbent action, as measured by the methylene blue test
- 2 Its neutralizing action continues for several hours even in the presence of an excess of acid and exerts a sustained control over gastric hyperacidity
- 3 This prolonged neutralizing action enables a minimum amount of mineral base to control hyperchlorhydria continuously. The quantity required is far below that which has been known to produce toxic symptoms of alkalosis. The trisilicate itself is insoluble in water and

weak alkalis, so that any unused excess remains unabsorbed

- 4 In the presence of acid the trisilicate acquires a gelatinous consistency, and if any of the mass lodges in the ulcer crater it will progressively neutralize the acid which diffuses through it
- 5 It has strong antipeptic powers available for the protection of the ulcer base from destructive digestion.
- 6 It can be given in large doses without disturbing the general motility of the digestive tract. It does not cause either constipation or diarrhea
- 7 Being completely insoluble in water any unused excess is voided in the stools, so that it cannot be absorbed and so produce direct alkali poisoning

MANDELIC ACID

Therapeutics—The use of acid in infections of the urinary tract came as a direct outgrowth of the excellent results in treating such infections by careful administration of the ketogenic diet Rosenheim, in search for an acid similar to betahydroxybutyric acid, which was proved to be the bactericidal factor of ketonurine came on mandelic acid. He tound mandelic acid would exert a definite bactericidal effect on the urine when given in sufficient dosage providing the urine was highly acid.

Dosage—F N Cook,⁴⁰ reporting on the use of mandelic acid in 500 cases of urinary tract infections, gives the dose of the drug as 1 ounce (30 cc) of the solution, (3 Gm of the acid) four times a day. With the advent of the newer preparations of the drug, the original dose of 12 Gms of the acid must be maintained and regulated according to the concentration of the solutions used. The most satisfactory results, the author claims, have been obtained by administering the drug in the prescribed dosage.

for a period of 6 to 12 days. If the urine is not free of bacilli at the end of this period it is better to discontinue administration of the drug for 10 to 14 days and then institute a second course of treatment This prevents the possibility of the organism from building up a tolerance to the drug and also lessens the danger of renal irritation from the drug Two points are essential in satisfactory management of patients undergoing this form of therapy The amount of fluid ingested in 24 hours must be limited to 1200 cc or less, and every effort must be carried out to maintain a urinary pH of 55 or below. With the newer preparations of ammonium mandelate the urine will maintain the desired level of pH without the use of ammonium nitrate or chloride, hydrochloric acid or the ketogenic diet Some cases, however, require these secondary acidifiers to maintain the urine at a sufficiently high acidity

Cook reports that 80 per cent of the uncomplicated cases of bacillary infection of the urinary tract respond to this form of therapy. As a preliminary to instrumentation or surgical treatment of the urinary tract, administration of the drug is frequently of value, even though elimination of the infection is not accomplished.

Results—A summary of the first 15 cases of infection of the urinary tract treated with mandelic acid at the Massachusetts General Hospital is given by F H Colby 41 The results of treatment showed that seven of the patients became free of their infection in a week or less This means that the urine contained no pus and was sterile on culture and the patient was symptom-free Complicating factors in five cases, such as prostatic infection, enlarged prostate and bladder diverticula were present and constitute

unfair tests of any urinary antiseptic Therefore, the acid was effective in sterilizing the urine, in seven of ten individuals or in 70 per cent. The treatment failed in two cases in which it was reasonable to expect success.

H F Dietrich⁴² reports on a series of 16 infants and children suffering from acute and chronic urinary infections, who were treated with sodium mandelate and became sterile in from three to ten days after institution of the treatments and remained sterile during the rest of the patient's stay in the hospital In favorable instances the urine was strongly bactericidal, some organisms other than bacillus coli-communior and bacillus colicommunis are killed by urine containing mandelic acid In four (25 per cent) of the patients evidence of renal irritation appeared after institution of the treatment and disappeared when sodium mandelate was omitted

E Schnohr and C Johansen⁴³ report the treatment of 23 cases with *pyelitis* and *cystitis* treated with mandelic acid. The authors report that the urine become sterile in from 3 to 30 days. In the remaining cases the drug had to be stopped, in two after two days, because of untoward effects. In eight cases described later which as a whole had more marked urinary infection, calcium amygdalate was given, which is tasteless and does not upset the digestive tract. The therapeutic effect was equally as good as that attained with sodium amygdalate.

Untoward Effects — In regard to renal irritation resulting from mandelic acid therapy, W F Braasch⁴⁴ found that approximately two per cent of more than 500 cases treated with mandelic acid showed evidence of temporary renal irritation, as evidenced by the finding of red blood cells or a few hyaline casts in the urine Gross hematuria was ob-

served in only two cases following mandelic acid therapy. When these untoward symptoms appear, they usually disappear within three or four days and seldom persist after the drug is stopped.

METHYL CHLORIDE POISONING

Two cases of methyl chloride poisoning with recovery are reported on by A Weinstein,45 resulting from exposure to the gas while repairing an air conditioning apparatus Methyl chloride is a nonirritating odorless gas with a low boiling point (237 C) The low boiling point of the gas plus many other advantageous features has caused it to be used extensively as a refrigerant However, the fact that it is practically odorless, and nonirritating makes the gas a very treacherous one from the standpoint of an industrial hazard. The histories of the two patients reported on by the author show that one man was exposed to the gas for a period of approximately two hours, while the second man remained two additional hours. The early symptoms of exposure consisted of headache, dizziness and tatigue. Later symptoms consisted of abdominal cramps, nausea and vomiting, simulating food poisoning. No change in pulse rate or blood pressure was noted and no cyanosis was present. Blood urea nitrogen was elevated in both cases and one case showed a reduction of chlorides and carbon dioxide combining power of the plasma Two characteristic features of this type of gas poisoning are the odor of the breath, which is strikingly similar to that of chloroform and the presence of formic acid in the urine. It has been shown that the quantity of formic acid excreted parallels the severity of the intoxication.

MORPHINE SULFATE

Therapeutics—C J Betlach⁴⁶ states that although morphine sulfate has been used therapeutically for about 135 years, very little has been written concerning the very effective results obtained when the drug is administered intravenously From the experience of the author with the use of morphine sulfate by both the subcutaneous and intravenous route, there are certain definite advantages obtained by giving the drug intravenously The full analgesic effects are obtained immediately (2) The drug can be given the moment it is needed (3) The dose may be regulated accurately Experimental work dealing with elimination of morphine from the blood stream following subcutaneous and intravenous medication indicate that, although the immediate effect following intravenous use is more pronounced, the effect will probably last almost as long as the effect after subcutaneous administration The sensations described by patients who have received morphine sulfate intravenously are variable. Some complain of dizziness, tinnitus, tachycardia and a feeling of warmth Fainting with a quick recovery occurs rarely. Vomiting is less likely to tollow intravenous injections than subcutaneous administration, probably because the vomiting center is depressed more rapidly. At the Mayo Clinic the author states intravenous injections of morphine sulfate have been used mainly as an adjunct to regional anesthesia and for its analgesic effect in peroral endoscopy It is also a valuable aid in deep cervical block, brachial plexus, sacral block and other methods of regional anesthesia The author states that for bronchoscopy and gastroscopy morphine has been given intravenously more than 600 times during the last year from trauma, visceral colics and cardiac pain are cited as instances where pain can be controlled much more quickly by the intravenous injection of morphine than by the subcutaneous administration. For preoperative medication morphine may be given intravenously in emergencies, or when the regular preoperative dose of morphine has been forgotten

Dosage—For intravenous medication the author recommends ampules of a sterile solution of morphine sulfate. However, tablets of the drug are quite satisfactory if ampules are not available. One-sixth or 1/4 grain (10 or 15 mg) of morphine sulfate is dissolved in 15 or 2 cc of sterile water, respectively This is put in a 2 cc hypodermic syringe and a 20 or 22 gauge intravenous needle 1s attached About 1/24 grain or 025 to 033 cc of the solution, is injected first and 20 to 30 seconds are given, during which time any idiosyncrasy to the drug will be noted if it is going to appear The remainder of the drug is then injected until the desired effect is obtained

PAPAVERINE HYDRO-CHLORIDE

Therapeutics-Further evidence of the value of papaverine hydrochloride ın overcoming arterial spasm was demonstrated by S Perlow and L Bloch,47 who utilized the alkaloid in the treatment of a patient with spasm and possibly beginning organic occlusion of the arteries of both feet with impending gangrene due to ergotamine tartrate patient was given ½ grain (003 Gm) of papaverine hydrochloride, dissolved in 15 minims (1 cc) of physiologic solution of sodium chloride intravenously The following day ½ grain was given by mouth and four hours later ½ grain was Examination 12 given intravenously hours after treatment was begun revealed a marked improvement in the circulation and condition of the feet. The treatment was continued with two additional ½ grain doses of papaverine hydrochloride intravenously at six-hour intervals and finally three ½ grain doses of the drug were given during the next two days. The results obtained in this case of marked arterial spasm with impending gangrene within 12 hours after starting the use of papaverine hydrochloride were so dramatic as to leave no doubt in the minds of the writers as to the efficacy of this drug as a vascular antispasmodic

OUININE

Therapeutics — W A Smith⁴⁸ describes the use of *quinine* in three cases of myotonia congenita with results equally as remarkable as those obtained by A Wolf,⁴⁹ who is credited with first using quinine in four cases of the same disease

Smith gave quinine dihydrochloride $7\frac{1}{2}$ grains (0.5 Gm) to a 19-year-old youth suffering from myotonia congenita. In 30 minutes there was practically complete disappearance of all myotonic symptoms, including the myotonic reaction on electrical stimulation. The oral administration of $7\frac{1}{2}$ grains twice daily has been found to be sufficient to maintain freedom from symptoms.

Two sisters with similar, but milder symptoms were treated with 5 grains (0.3 Gm.) of quinine daily and obtained relief

SILVER NITRATE

Therapeutics — M Kissmeyer⁵⁰ reports on the use of a silver nitrate ointment for the treatment of burns of all degrees for the last 25 years. The formula used by the author consists of 0.25 Gm of silver nitrate, 25 Gm of distilled water, 50 Gm of hydrous wool fat, 25 Gm of olive oil. The ointment

is spread on a soft cloth and applied directly to the injured skin, after having been cleansed with sterile salt water, and all blisters removed. The area is then covered with oil cloth and bandaged The author claims that the ointment renders the wound painless even during changes. This form of treatment is particularly suited for infants and children, giving their lesions an antiseptic medium without injury to the newly forming skin.

SODIUM BENZOATE

Therapeutics — L Quaranta⁵¹ reports on the results obtained by administering sodium benzoate for the control of cough in pulmonary tuberculosis The author uses daily intravenous injections of 5 cc of a 25 per cent solution of sodium benzoate for 15 consecutive days and the treatment can be repeated every ten days. Small doses of 1 cc of the 25 per cent solution of sodium benzoate are first given intravenously for two consecutive days to test the tolerance of the patient The author reports the drug has an antiseptic action on bacteria associated with tubercle bacilli in the sputum and inhibits the action of the vagal sympathetic nervous ends that control bronchial secretion. The quantity and quality of the sputum are favorably modified, the attacks of coughing diminish in number and frequency and the general condition of the patient improves Seven or eight injections are usually necessary before satisfactory results are noticed The author reports about six per cent failures in a large series of cases

L Goldkorn⁵² reports on his experience with sodium benzoate in treatment of pulmonary suppurations and gangrenes The author uses 2 Gm or 10 cc of a 20 per cent solution intravenously

five to ten times In cases with more abundant sputum the dose was increased to 3 or 4 Gm, and as high as 4 to 8Gm twice daily have been used by the author A permanent cure of 18 patients with pulmonary abscess was obtained. In six cases of gangrene the results were remarkable in from five to six days The antiputrid action of sodium benzoate in doses of 8 to 16 Gm made the unpleasant breath disappear completely In four recent cases the cure was permanent Thirty per cent of the cases complained of flashes before their eyes and dizziness for a very short time following injections A few patients experienced transient pains in the abdomen

SULFANILAMIDE

The past two years have witnessed the introduction into medicine of a startling, new chemotherapeutic agent, sulfanilam-At the present time experimental and clinical observations which have led to the use of sulfanilamide or its derivatives in the treatment of certain infectious diseases show that the chemicals have powerful chemotherapeutic effects in both experimental and human infections Its great promise has initiated an extensive investigation and what appeared at first to be a chemotherapeutic agent specific for hemolytic streptococcal infections, is a drug possessing a broad chemotherapeutic valency

Therapeutics—At the present time the clinical and experimental evidence is sufficient to warrant the use of sulfanilamide or "prontosil solution" in the treatment of hemolytic streptococcal infections. Some of the specific illnesses in which the streptococcus is the offending organism and which, according to recent literature, sulfanilamide has been proven very useful are erysipelas, streptococci septicemia, streptococcic tonsil-

litis, complications following scarlet fever, acute or chronic osteomyelitis of streptococcal origin, and puerperal fever, when due to B hemolytic streptococcus. The status of sulfanilamide as a chemotherapeutic agent in pneumococcal infections is still inconclusive according to F F. Schwentker ⁵³ Experimental work has shown that the drug is at least bacteriostatic, if not bactericidal and that its effect varies with different types of pneumococci Best results have been obtained with type III infections

J H L Heintzelman, P B Hadley and R R Mellon⁵⁴ report nine cases of type III pneumonia treated with sulfanilamide, with seven patients recovering and two deaths. In a corresponding group of ten patients observed approximately during the same period, but not receiving sulfanilamide treatment, two patients recovered and eight died The conclusions of the authors were, that despite the small number of cases treated the difference in relative mortality in the treated and untreated groups appears to justify continued application of the treatment of type III pneumonia by sulfanılamıde

Schwentker (loc cit) states that preliminary experimental work with mice has shown that sulfanilamide affords these animals even greater protection against meningococci than against streptococci The author reports 52 consecutive, unselected cases of meningococcic meningitis treated with sulfanilamide alone, without antiserum tality in this group was 15 per cent, as compared to a 30 per cent mortality among serum-treated cases seen during the same epidemic in the same hospital Experimental work has further shown, according to the author, that when sulfanilamide therapy is combined with antiserum injections a synergistic effect apparently takes place The protection of mice against meningococci by the combined treatment is far greater than one would expect from the protection afforded by each method alone. Further clinical trial is needed to establish the best method of treatment.

Clinical evidence alone supports the use of sulfanilamide in gonococcal infections J. E Dees and J A C. Colston,⁵⁵ from their results in the treatment of 19 cases of gonococci infections conclude that sulfanilamide will prove of great value in this type of infection

Sulfanilamide has been used by H R. Bohlman⁵⁶ in the treatment of three cases of gas gangrene Marked clinical improvement was noted in all three cases within 24 hours after sulfanilamide therapy was instituted and Bohlman concludes that sulfanilamide appears to be a valuable adjunct in the treatment of gas gangrene

Dosage and Administration — A simple biochemical method for the quantitive determination of sulfanilamide in body fluids has recently been described by E K Marshall, Jr. K Emerson and W C Cutting 57 They have noted, following a single oral dose in human beings, that the drug is absorbed in about four hours and that a maximum concentration is reached in the blood stream within four to six hours These observations have been of the greatest importance in establishing a rational basis for therapy in infected human beings The dosage of sulfanilamide should be sufficient to produce and maintain in the tissue fluids, particularly those at the site of infection, a therapeutically effective concentration of sulfanilamide

P H Long and E A Bliss⁵⁸ state that sulfanilamide per os is the drug of choice If, however, the patient cannot swallow tablets or oral administration of the drug is not desirable, then either "prontosil solution" or an 08 per cent to one per

cent solution of sulfanilamide in sterile physiological saline solution may be used These solutions are given parenterally by the subcutaneous route

In patients ill with very severe infections, such as hemolytic streptococcal meningitis, peritonitis and septicemia or in meningococcal meningitis or septicemia the toxic effects of the drug should be disregarded, according to Long and Bliss, and a large initial dose of sulfanilamide administered with the aim of attaining a blood level of 10 mg per cent within four hours Patients weighing 100 pounds or more, may be given an initial dose of from 10 to 16 5-grain tablets This dose should give a blood level of about 10 mg per cent within four hours Then, to maintain this level, three 5-grain tablets every four hours may be given If the patient's weight is 50 to 90 pounds, the initial dose should be six to ten 5grain tablets followed by two or three tablets at four hour intervals. In children weighing 25 to 50 pounds, four to six 5-grain tablets constitute the initial dose, followed every four hours by doses of one or two 5-grain tablets. Blood sulfanilamide levels should be determined four hours after the initial dose and if the blood does not show the expected level of 8 to 10 mg per cent, this is evidence of faulty absorption and the parenteral administration of the chemical Also, it is of value to should be tried have a 24 hour check on the blood levels to determine the adequacy of the maintenance dose of the drug. In the use of parenteral sulfanilamide solutions Long and Bliss state that the following amounts represent adequate therapeutic doses

In adults, the initial hypodermoclysis should be 500 cc of one per cent solution, followed by 300 cc at eight hour intervals. Individuals weighing 50 to 90 pounds should receive 200 to 400 cc

of a one per cent solution and followed by 200 cc at eight hour intervals Children weighing 25 to 50 pounds should receive 100 to 300 cc of sulfanilamide solution, followed by 100 to 200 cc at eight hour intervals

Babies should receive a total of 1 gram of sulfanilamide per ten pounds of body weight during the first 24 hours Sulfanilamide may be given by the intrathecal route in the treatment of meningococci meningitis and of streptococcal infections of the meninges. The technic of administration is the same as that used in giving antisera by this route. The solution should never be injected under positive pressure. Intrathecal therapy may be given at eight hour intervals.

"Prontosil solution" should be given by the subcutaneous route. It is absorbed rapidly and is practically nonirritating In adults the therapeutic dose of "prontosil solution" is 20 cc at four hour intervals or a total of 120 cc of the solution in 24 hours. Individuals weighing 50 to 90 pounds should receive 5 to 10cc every four hours "Prontosil solution" should not be administered intrathecally as it is definitely irritating and severe reactions may follow the intravenous use of the drug definitely favorable clinical effects have been observed in the patient, the dose of sulfamlamide should be rapidly decreased At first the dose may be cut by one-third If the patient's condition improves further the drug should be cut to one-third of This should be the original amount continued until convalescence is well established Moderately severe streptococcal infections in adults may be contiolled by the administration of three 5 grain tablets of sulfanilamide at four hour intervals, while mild infections require one or two tablets at the same interval.

Toxic Effects of Sulfanilamide and Its Derivatives

Sulfanilamide is a toxic chemotherapeutic agent and its widespread use will result in many fatalities unless the tendency towards its careless and reckless use is checked. Already fatalities attributed to the use of sulfanilamide or its derivatives have been reported by L D B Frost ⁵⁹

The total experience thus far gained in the use of sulfanilamide is not sufficient to establish the exact status of its toxic effects. Certain unusual symptoms may develop during the course of treatment, and according to Schwentker (loc cit), consists of a feeling of light headedness usually described as "whoozy" or drunk. Associated with this may be ringing in the ears, headache, a slight temporary loss of mental acuity and at times tingling or other paresthesias.

The commonest toxic manifestation according to the author is cyanosis It varies from an almost imperceptible blucness of the mucous membranes to a deep cyanosis The condition appears to be relatively harmless. The mechanism of the cyanosis is not yet clear, in severe cases it appears to be due to sulphemoglobinemia About six per cent of patients receiving sulfamlamide develop a rash, according to Schwentker, normally appearing between the tenth and fourteenth days of therapy Wlen a rash develops the drug should be stopped, and the eruption usually fades rapidly Occasionally fever develops during sulfanilanide therapy If possible the drug should be discontinued, but in very severe infections it may be necessary to ignore the fever and continue the use of the chemical to combat the infection. Acidosis, in some degree, develops in practically all patients receiving sulfanilamide therapy Rarely the CO2 combining power for

the blood, falls to 20 volumes per cent, usually it is between 35 and 40. Sodium bicarbonate by mouth or sodium lactate solution parenterally will usually combat the acidosis. As a preventive measure sodium bicarbonate may be administered with the sulfanilamide.

Acute hemolytic anemia is another not infrequent toxic manifestation sulfanılamide therapy Very often the drop in the red blood cell count and hemoglobin are very rapid Schwentker reports patients whose hemoglobin fell from 85 to 30 per cent in three days The drug should be stopped on the appearance of anemia, unless the need is urgent, then transfusions may be used to control the hemoglobin level while treatment with sulfanilamide is continued Other more rare toxic manifestations are granulocytopenia, which is a rather serious complication and makes it imperative to follow the blood leukocyte count at least every two days Taundice also occurs during treatment, with the drug, but very little is known of the exact nature of this toxic manifestation

COMPOUND SOLUTION OF TANNIC ACID

Therapeutics—The life-saving qualities of the tannic acid crust therapy in the treatment of extensive burns is recognized by everyone today. Prior to the discovery by E C Davidson, burns involving more than one-third of the body surface were invariably fatal Now lives are saved when burns involve more than one-half of the body surface There has been a considerable lack of uniformity in the technic in carrying out the treatment with the result that many general complaints have arisen. One of the chief difficulties encountered in extensive burns is sepsis appearing beneath the tannic acid crust in the course of several days

Also, the production of a good firm crust, is obviously the aim of the treatment, but various writers have advised the use of varying strength of solution to obtain the best crust formation. Solutions of tannic acid in water varying from 2.5 per cent to 20 per cent have been recommended

B Fantus⁶⁰ devised a solution that has definite advantages over the tannic acid solutions in water, and from the results of the experimental work carried out by the author should give uniformly better results in the treatment of extensive burns

The advantages of this compound solution of tannic acid as given by the author are

- 1 It is endowed with good keeping qualities
- 2 It produces a denser coagulum
- 3 It has bacteriostatic action

FORMULA

Compound Solution of Tannic Acid
Potassium chloride 0 42 Gm
Calcium chloride 0 84 Gm
Salicylic acid 1 00 Gm
Sodium chloride 10 50 Gm
Tannic acid 100 00 Gm
Distilled water to make 1000 cc

Mix and permit to stand with occasional agitation until dissolved and filter, it required, to dispense a clear solution

The author also recommends that ten per cent silver nitrate solution be applied to the tannic acid crust

UREA

Therapeutics—H G Holder and E. M MacKay⁶¹ report on the results obtained in the use of urea, in the treatment of infected wounds From the experience derived from treating 139 cases the authors state that the application of large quantities of urea crystals or of strong to saturated aqueous urea solutions to infected wounds definitely

hastens healing and is frequently effective when other local measures have failed The treatment is cheap and apparently causes no irritation of surrounding tissues and it also obliterates practically all the odors arising from an infected wound. The mechanism of urea therapy is due in part to the bactericidal effect of strong urea solutions (evident in solutions above 30 per cent concentration), and chiefly through the solvent action on proteins, which leads to the removal of débris, incrustations and dead tissue The results in many of the author's cases were very striking, both in long standing lesions and in more recent conditions Urea is practically nontoxic and harmless and may be used in any reasonable quantity

R B Lewy⁶² reports on the use of urea in diseases of the ear, nose and The conditions in which beneficial results were obtained were carcinoma, Ludwig's angina, maxillary sinusitis, cervical adenitis otitis media and mastoid wounds The author found a two per cent solution of urea beneficial in reducing metastases in certain types of infected necrotic carcinoma. Its value for infected wounds of the ear and thioat and infected wounds of the neck and the floor of the mouth equals the good results obtained in treating infected wounds in other parts of the body. Its specific effects seem to be elimination of odor, proteolysis of necrotic tissue and stimulation of granulation and epithelization

VENOM (SNAKE)

Therapeutics—The effectiveness of the venom of Russell's viper in controlling three cases of postoperative bleeding is recorded by J B Hance ⁶³ In the first case (tonsillectomy) a 1 10,000 dilution was applied locally on swabs and the oozing stopped at once. In the

second case two intravenous injections of 0.5 cm. 1 100,000 dilution were employed as a desperate measure (because the preparation used was labelled "not for injection"), in a case of severe bleeding and collapse after hysterectomy The patient recovered, aided by transfusion In the third case an intradermal intection of 0.5 cm of 1 100,000 dilution was given as a prophylactic to a man known to be a "bleeder," before an operation on the gallbladder, after the operation another injection was given and the slight oozing which had taken place stopped The venom used in America is obtained from the moccasin snake. Injections of 0.2 to 1.0 cm of a 1 3000 solution have been found effective in controlling various hemorrhagic conditions not associated with blood changes Moccasin venom differs from Russell's viper venom in that it has no effect in congenital hemophilia

E J Davin, F Spielman and J A Rosen⁶⁴ report on the use of moccasin snake venom in 51 cases of puerperal hemorrhage, in all of which the period of bleeding was materially shortened

M A Goldberger and S M Peck⁶⁵ report the use of venom in 17 cases of functional uterine hemorrhage with good results They also tried it in five cases of bleeding due to fibroids but found it meffective They suggest that the venom acts directly on the uterine capillaries S M Peck, N Rosenthal and L A Erf66 discuss the value of moccasin snake venom as a diagnostic, prognostic and therapeutic agent in purpura The exact nature of the purpuric manifestation, generalized or local, as well the trend of the purpuric state can be determined by the venom test, which furnishes a clear indication of capillary fragility An intradermal injection is made of 0.1 ccm of a 1 3000 dilution of venom, with a control injection of normal saline solution and the reaction is noted after an hour. A positive reaction is indicated by capillary rupture with diffusion of blood into the tissues. Change from a positive to a negative reaction indicates clinical improvement. Subcutaneous injections of diluted venom given twice a week in gradually increasing doses proved of value in a number of cases of purpura hemorrhagica.

VITAMINS

R A Peters⁶⁷ in a discussion of "The Use and Abuse of Vitamins," states that the only object of separate dosing with vitamin (apart from that already in food) is to raise the daily ration to the minimum amount required However, it must be realized that the vitamin content of food may vary, not only in relation to the quality of food, but also cooking, storage and other factors difficult to control cause variations Therefore, it is wise to give a margin of vitamins to cope with possible fluctuations in the diet of overdosage need not be feared in dealing with the water-soluble vitamins such as those of the B class and vitamin C (antiscorbutic), because excess is likely to be excreted in the urine

With fat-soluble vitamins such as D there is a possibility of overdosage, although it is probably seldom seen in practice. Marked idiosyncrasy to the vitamins also exists in many cases, requiring much larger doses to control a given condition than would ordinarily be needed. The author also draws attention to the fact that when vitamins are given by mouth they may or may not be properly absorbed, or may be destroyed in the intestine. In other words, it is possible that a considerable number of deficiency states will be found to arise as a result of abnormalities of digestion and

alimentation. More emphasis is constantly being placed on the fact that changes in the gastrointestinal tract which lead to failure of adequate absorption may lead to deficiency diseases even though the diet is adequate in vitamins.

In patients suffering from acute vitamin deficiencies proper vitamin therapy should induce a rapid change. If, however, the deficiency is of a more chronic nature then there may be a long delay in improvement since tissue repair will take a correspondingly long time. In most cases in from two weeks to a month there should be some noticeable improvement. Cases failing to respond to vitamins by mouth should be given a trial by injection, where this is possible. If after a reasonable time injection has no effect, there appears to be no sense in continuing to dose with vitamin

Therapeutic Indications

Vitamin A $(C_{20}H_{30}O)$ — Peters states that deficiency of this vitamin is regularly associated with the appearance of intections, such as bronchitis, in the The vitamin is a colorless laboratory. oil, found in fish oils associated with vitamin D, and is especially abundant in halibut liver oil. The vitamin is stored in the liver. It protects mucous surtaces such as the conjunctiva from the entry of toreign organisms and is also a constituent of visual purple, the diseases of keratomalacia and of hemeralopia being associated with it Vitaniin A is indicated as a protection against infection, as a cure in certain eye diseases and also in obscure nervous diseases involving degenerative changes Tests for the vitaniin have been developed which depend upon the speed of accommodation to dark conditions

H Jeghers⁶⁸ discusses the prevalence of vitamin A deficiency in a group of supposedly normal adults and concludes that night blindness (hemeralopia), in the absence of intra-ocular disease, is the earliest and most constant manifestation of vitamin A deficiency in adults. The author states that vitamin A deficiency may occur even if the amount ingested daily is theoretically adequate if any condition is present which (1) increases the metabolic need for vitamin A, (2) interferes with the proper absorption from the gastrointestinal tract, or (3) interferes with the conversion of carotene or storage of vitamin A in the liver Vitamin A deficiency is considered by some to be associated with rather characteristic cutaneous lesions and since the principal influence of vitamin A is on epithelial tissues, this might be anticipated characteristic change consists of keratinization of a hard, dry papular type most marked on the extensor surfaces of the forearms, legs and thighs The relation of vitamin A to infections is discussed by D L Wilbur,69 who states that the most important practical problem in this respect is not so much whether a person who is receiving an inadequate diet is less capable of resisting infection than is a normal person, but whether by increasing the vitamin A intake above that normally received by the average well individual will further increase his resistance to infections According to the author there is no known influence on immunologic processes associated with vitamin A and the only anti-infective influence it possesses is in maintaining normal epithelium, which will act as a barrier to infection The author concludes, therefore, that vitamin A in reality is not an anti-infective vitamin, as it has been termed by many writers

Vitamin B_1 ($C_{12}H_{17}ON_4S$.-ClHCl)—The vitamin B complex now consists of several parts, vitamin B_1 being the only one that is certainly applicable to man Vitamin B_1 which is also

known as oryzanin, torulin and aneurin is the base of pyrimidine type containing sulfur and has now been synthesized The vitamin is water-soluble and is not stored in large amounts in the body. It is connected with the intermediary metabolism of carbohydrates and is probably a universal constituent of cells. Vitamin B₁ cures the condition of beri-beri and should be tried in cases associated with a loss of appetite. Edema, breathlessness, anorexia nervosa, neuritis and painful muscles according to Peters, are other conditions in which evidence exists that vitamin B₁ is indicated Patients who do not respond to vitamin B therapy by mouth should always have a thorough trial of this factor by intravenous injection before deciding that the condition is not due to a vitamin deficiency The author recommends an amount corresponding to at least 5 to 10 mgm of the pure vitamin (Approximately 5000 international units should be given in any trial)

R Tislowitz⁷⁰ found that the parenteral administration of vitamin B_1 reduces the fasting blood sugar of normal rabbits and dogs and that the hyperglycemia of dogs after dextrose tolerance tests is likewise reduced following the administration of vitamin B1 It is assumed by the author that vitamin $B_{\mbox{\scriptsize 1}}$ has a point of attach either in the hypophysis or in the central nervous system The author also suggests that the beneficial action of certain vegetable diets on diabetes mellitus might, among other factors, be due to the content in certain vitamins The use of vitamin B₁ is suggested in delirium tremens

S Weiss and R W Wilkins⁷¹ reported that there are certain changes in function of the cardiovascular system in vitamin B_1 deficiency. The disturbances of cardiovascular function described by the authors are dependent

partly on changes in the nervous system and partly on changes in the myocardium and the vascular system Various combinations of the following changes were noted, simple tachycardia, vagus reflex, irritability with bradycardia or with asystole and syncope, right-sided and left-sided heart failure, peripheral arteriolar dilatation and vasomotor collapse with vascular constriction

Vitamin G (B₂)—Since it has been proven that vitamin B is composed of several separate fractions, there has been much interest in the character and physiologic properties of the antidermatitic factor, B₂ or vitamin G One of the chief controversies concerning this vitamin is its relation to pellagra Some authors believe pellagra is a pure avitaminosis B, or B₂

C A Aldrich⁷² in a discussion of this factor (B₂) states that pellagra can be prevented by administering vitamin G, and the disease frequently occurs in those living on diets poor in this factor. In recent cases of pellagra, treatment with vitamin B₂ has been successful, but in cases of long standing, with nerve and cord degenerations taking place results with vitamin therapy have been disappointing

Vitamin C (C₆H₅O₆) — Vitamin C which is the antiscorbutic principle of orange juice is water-soluble and therefore not stored in the body to any extent The factor has been synthesized, is highly reducing and is not stable in neutral or alkaline conditions Therapy is indicated in cases in which orange juice is unacceptable or when more rapid action is desired. While the relation of vitamin C to the prophylaxis and treatment of scurvy need not be discussed, considerable interest lately has been given to "latent" or "preclinical" scurvy D L Wilbur⁷³ describes the clinical features of this condition as in-

cluding dental caries in children, a hemorrhagic tendency which may manifest itself in hemorrhage from any organ, subcutaneous petechiae, a positive capillary resistance test, and a variety of indefinite symptoms fatigue, pallor, underweight, and frequent infections. According to the author it is still a much discussed, but unanswered question whether or not cases of isolated idiopathic hemorrhages from the nose, gastro-intestinal tract, urinary tract and other tissues can be related to vitamin C deficiency when no other evidence of deficiency of this factor exists in the body The methods of determining the presence or absence of partial deficiency of vitamin C are given by Wilbur as (1) the use of capillary resistance tests, (2) estimations of the content of vitamin C in the blood and urine, and also, a therapeutic test in which ascorbic acid 15 given which may produce presumptive evidence of deficiency

J F Wilkinson and C A Ashtord⁷⁴ discovered a vitamin C deficiency in three cases of Addison's disease by the unne titration method. There was a subnormal concentration of cevitamic acid in the urine and very low 24-hour excretion during the control period. This was followed by responses of varying degrees, to the repeated oral administration of large test doses of the one-cevitamic acid. When therapy was stopped, the increased excretion fell rapidly to values characteristic of the control period The pigmentation of the cases reported did not show any appreciable change during the test period of intensive oral cevitaniic acid therapy

T H Lanman and T H Ingalls⁷⁵ report on the healing of operative incisions made on guinea pigs who were partially depleted of their cevitamic acid depot. The animals were subsequently maintained on approximately one-fifth

of the minimal protective daily dose of cevitamic acid The healing of the operative incisions of these animals, both histologically and physiologically, was inferior to that of a group of control animals The wounds of the scorbutic group ruptured at a pressure averaging about one-third that required to rupture the wounds of normal animals The authors conclude that the administration of cevitamic acid is justified in operative cases who have or are suspected of having a low cevitamic acid depot The relation of vitamin C and pigmentation of the skin has been studied by T. Cornbleet 76 He finds that pigment is increased in the skin when the depots of vitamin C in the adrenals are depleted The excess pigment in the skin in Addison's disease and in scurvy is absorbed when vitamin C is administered Pigment and vitamin C occur together in the skin, pigment acting apparently as the anchor that holds the vitamin If pigment is not present vitamin C is not stored in the skin Copper hastens the darkening and precipitation of dopa by ultraviolet Vitamin C retards the precipitation Lack of vitamin C accelerates the production of pigment

Vitamin D $(C_{29}H_{44}O)$ — Vitamin D is derived from ergosterol and is known as calciferol, or in this country as viosterol The compound is a close approximation to, but is not a pure vitamin The factor is fat-soluble and is therefore stored in the body Physiologically, the vitamin is concerned with absorption of calcium and phosphorus from the gut, having to do with the retention of calcium and phosphorus in the body and in the deposition of calcium and phosphorous in the bones, so that their level in the blood stream is sufficient for normal osteogenesis Wilbur states that deficiency of vitamin D may be suspected in persons with dental caries, tetany, and frequently occurring fractures. There are also indications that in persons suffering from disorders of intestinal absorption such as sprue and celiac disease vitamin D deficiency may be present. Deficiencies due to this factor are encountered much more frequently in children than in adults, the occurrence of vitamin D deficiency states in adults being extremely uncommon, according to Wilbur

Dosage and Administration of Vitamins

In the use of the vitamins as a prophylactic against deficiency disorders, and in the treatment of deficiency states when they exist Wilbur recommends the following measures:

Vitamin A-The daily requirement of vitamin A is not definitely known, but is probably somewhere between 6000 and 10,000 USP units By using adequate amounts of foods rich in vitamin A such as butter, cream, cod liver oil, carrots, eggs, and spinach deficiency states due to this factor are usually prevented In the presence of clinical vitamin A deficiency the following measures should be employed, (1) a diet with a high vitamin A content, (2) the use of cod or halibut liver oil or carotene in amounts equal to at least 10,000 U S P units, in extreme cases the use of intramuscular injection of cod liver oil or other similar substances

Vitamin B_1 —Many therapeutic methods are available at present in the handling of vitamin B_1 deficiencies Yeast, fresh vegetables, whole cereals, and milk are advised in the diet, because of their high content of vitamin B_1 Preparations of brewer's yeast in powdered or tablet form are available Crystals of vitamin B_1 , which may be given intramuscularly in solution or orally are available. The minimal therapeutic dose

of vitamin B₁ is probably about 10 to 20 mg daily Wilbur advises the use of yeast in place of, or in addition to, the crystalline form of B₁, because yeast contains all the factors of the water-soluble B complex. Twenty-five Gm of powdered brewer's yeast one or four times daily depending on the degree of deficiency, along with a high vitamin diet is advised in a state of clinical B₁ deficiency.

Vitamin C.—The diet should be abundant with fresh vegetables and citrous fruits. Synthetic crystalline vitamin C may be administered by mouth or intravenously; from 50 to 200 mg or more daily, should be adequate For intravenous use the sodium salt of cevitamic acid aproaching approximate isotonicity can be used One per cent of the salt dissolved in physiologic salt solution or three per cent dissolved in distilled water In case the acid only is available, it should be neutralized with half its weight of sodium bicarbonate in physiologic salt solution or water before it is injected

Vitamin D.—In regard to administration Wilbur gives the following methods concerning vitamin D. It may be given in fish oils, such as cod liver oil, and in a variety of foods, such as milk and cereals. Ultraviolet light exposures will produce vitamin D in the skin. In the treatment of rickets the author states that 20 drops of viosterol (4500 U.S. P. units) constitute approximately a therapeutic dose. In adults suffering with senile osteoporosis, ten drops of viosterol three times a day with 4 Gm of calcium lactate three times a day will often relieve the symptoms.

ZINC SULFATE

Therapeutics—E W Schultz and L P Gebhardt⁷⁷ experimented with 40

different chemical agents, applied to the olfactory mucosa of monkeys, with the idea that certain chemicals might modify the permeability of the mucous membrane to the virus of poliomyelitis From their notes, the authors announce that zinc sulfate, which because of its simple composition, relatively low toxicity and surprisingly high protective action in monkeys seems to deserve a trial in man

Procedure-In carrying out the work in man, the following procedure is suggested by the authors:

- 1 The use of a solution containing one per cent zinc sulfate, 05 per cent sodium chloride and one per cent local anesthetic (pontocaine)
- 2 The solution should be prepared with U S P zinc sulfate, U S P sodium chloride and distilled water
- 3 It should be applied at least once every two weeks during times when the risk of infection is great. A more desirable procedure would be to apply the agent on two or three successive days, and once every two weeks thereafter
- 4 It should be applied with an atomizer equipped with a suitable tip and in accordance with the technic of M Pect D H Echols and H J Richter 75
- 5 Thorough application of the zinc sulfate according to the technic of Peet may be somewhat painful Therefore 0.5 per cent pontocame was added to the solutions, and experimental work in monkeys proved definitely that the anesthetic in no way detracted from the protective action of the zinc sulfate

Further laboratory studies may in time lead to a more satisfactory procedure, but Schultz believes the immediate task of the profession is to make the best possible use of the most promising practical measure now available for the control of this disease.

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PHYSICAL THERAPY

Edited by John S. Coulter, M D.

ELECTROTHERAPY

By John S. Coulter, M.D.

Short Wave Diathermy

Special Selective Thermal Action-As was stated in Service Volume XIII, 1936, page 966, Mortimer and Beard found no advantage of one wave length over another for heating purposes In Service Volume XIII, 1937, pages 934 and 935, it is shown that several studies by Coulter and Carter and Coulter and Osborne confirmed this statement

After making over 300 tissue temperature measurements on human subjects, Coulter and Osborne¹ came to the conclusion that in the heating of live human muscle and fat there were no significant differences in the use of different wave lengths from 6 to 24 meter wave lengths

Short Wave Therapy Without Heat Effect-Liebesny was the first to recommend a weaker dosage in short wave diathermy, and he named his method "The Athermic Short Wave Treatment" The aim of short wave therapy as recommended by him is the opposite of diathermy for the athermic short wave therapy avoids heating as much as possible Liebesny2 cites examples which he says prove that short waves have biologic actions that are the opposite of heat action

without producing heat effects

Weissenberg³ has devised a method which he named "Low Intensity Short Wave Treatment." This is another method of using short wave diathermy

Until further proof is offered, it is believed that the Council on Physical Therapy of the American Medical Association4 is correct in stating effects of common electric currents when applied to the body tissues may be thermal, chemical or mechanical in nature, depending on the physical characteristics of the current High frequency currents apparently avoid the mechanical and chemical effects but display the ability to heat the body tissues through which they pass At the present time it is believed that the local physiologic effects of the three methods of applying high frequency currents aforementioned are limited to the effects of the heat produced "

Specific Bactericidal Action-This was discussed in Service Volume XIII, 1936, page 966, and it was believed that the claims for this supposed action may be more rationally explained on the basis of point heating Claims for the specific bactericidal action of short wave diathermy are still appearing in the literature Wertheim⁵ states that in his experiments careful measures were taken to exclude the effects of heat He reviews the behavior of a number of bacteria and fungi in the short wave field, and finds the staphylococci and streptococci are rather sensitive. He concludes that his results prove once more the specificity of certain wave lengths In contrast to this, Menniti⁶ subjected cultures of living virulent tubercle bacilli to irradiation with short waves (eight meters) for two, four, six and eight hours Guinea pigs were given intraperitoneal and subcutaneous injections of irradiated and nonirradiated tubercle bacilli. The author concludes that short waves have neither an abiotic nor immunizing action on tubercle bacilli.

It is believed that the following conservative view of The Council on Physical Therapy of the American Medical Association should be accepted: "So far as competent investigators have been able to determine, there is no demonstrable, selective thermal action, or specific biologic or bactericidal actions in vivo that may be attributed to short wave diathermy. To date, the effects produced can be explained only on the basis of the generation of heat"

Specific Biologic Action — Mortimer and Osborne as mentioned in Service Volume XIII, 1936, page 966, state that there is no conclusive evidence from the literature nor were they able to substantiate the claims of specific biologic action of short-wave diathermy. In Service Volume XIII, 1937, page 934, attention is directed to the confirmation of this statement by Hill and Taylor, Wetzel and Kiesselbach, and Curtis, Dickens and Evans

Hill and Taylor⁷ give further experiments on a frog heart and a nerve muscle preparation to prove that there are no specific biologic actions of high frequency fields

Technic Short Wave Medical Diathermy—Short wave medical diathermy may be administered by two methods—electromagnetic induction and the electric field Coulter and Osborne⁸ give the following technic

Electromagnetic Induction Technic — In this method of administering short wave medical diathermy, the current is conducted to the patient by means

of a very flexible heavily insulated cable or by means of a disc electrode containing the cable coiled and positioned ready for treatment The cable is coiled about or around the part to be treated when the cable is used as the electrode Sufficient bath toweling must be interposed between the cable and the skin. Close proximity of any metallic or other conductive articles should be avoided when treatment is in progress so that the patient may receive the full effect. It is also usually necessary to provide a good ground for these machines The manufacturers of the particular apparatus used will designate whether a ground is necessary or not It is not advisable to use metal treatment tables Mattresses with inner springs should never be used as sufficient heat under certain conditions may be generated in the springs to ignite the mattress material An iron bed can be used provided the coil is kept at least a foot away from any portion of the iron framework A wooden chair is satisfactory where it is desired to give treatments in a sitting position The section of the cable between the plug in terminals of the machine should be separated at least four inches

The cable may be used in the form of a loop of one or more turns or in the shape of a pancake coil of one or more turns. The number of turns used may differ for various machines

Electric Field Technic—The technics accepted by the Council on Physical Therapy of the American Medical Association for the use of the electric field are the double cuff technic and the air spaced electrodes so applied that one electrode is proximal and one distal and both on the same surface as the part to be treated

The cuff electrodes are made of flexible metal plates vulcanized between two layers of rubber providing thorough electrical insulation, so that there will be no danger of the current arcing from the metal to the patient's skin These vary in size according to the characteristics of the various machines Sufficient bath toweling or felt must be interposed between the electrodes and the skin If too much padding is used, there will be too little internal heating and if insufficient is used, the superficial tissues will become too hot and burning is very apt to occur The electrodes should never be applied over clothing of any kind One must guard against the accumulation of pools of moisture, as perspiration between the patient and electrode will cause prickling, hot spots and, if not corrected, blisters Never disregard the patient's complaint regarding hot spots

The use of pad electrodes is the most inefficient technic for the deep heating of tissues with short wave diathermy. It is to be emphasized that the Council on Physical Therapy have not accepted this mode of application.

In applying the air spaced electrodes, the dosage, as with other methods, is regulated by the patient's tolerance. The ability to heat the deep tissues of the human thigh with air spaced electrodes appears to be dependent on the size of the electrodes, the energy available from the apparatus, the method of application, the distance of electrodes from the skin, and the patient's tolerance.

It is of the utmost importance to provide sufficient distance—a so-called air gap—between the patient's skin and the electrodes. Proper air spacing avoids the so-called skin effect, which if present may result in overheating of the skin and possibly burns. When the electrodes are not correctly spaced, about 80 per cent of the energy is used up in skin effect. This technic requires a machine with sufficient output to make it efficient.

The Council on Physical Therapy of the American Medical Association has accepted these electrodes as an efficient method of producing heat in the deep tissues when properly applied on the same surface of the part to be treated. Other technics in which the part to be treated is sandwiched between the electrodes are not of any value unless superficial heat is desired. Both electrodes must be on the same plane of the area to be treated to be effective.

Treatment of Peripheral Nerve Injuries and Infantile Paralysis

Chor9 has continued his work on this subject that was mentioned in Service Volume XIII, 1937, page 935, and states that a series of experiments was recently carried out at the Northwestern University Medical School by the authors and associates Using macaca rhesus monkeys, the gastrocnemius-soleus muscles were paralyzed by sectioning the sciatic nerve The severed nerve was sutured immediately following section to aid in establishing the best pathway for the regenerating nerve fibers. In one experiment both sciatic nerves were cut. One side received daily electrical stimulation ten contractions, galvanic current), the other no treatment. At the end of six weeks the treated side showed just as much atrophy as the untreated, indeed, there was slightly more wasting on the treated side

In another experiment, three groups of monkeys in whom one sciatic nerve had been severed and sutured were treated as follows. One group received daily electrical stimulation (ten contractions, galvanic current), another daily passive movement and massage and the third group rest by immobilization in a plaster cast. At the end of six weeks it was found that the amount of atrophy was practically the same in the three groups. In conclusion, therefore, the authors state that muscle atrophy follow-

ing nerve section in the macaca rhesus monkey progresses up to a period of at least six weeks despite treatment by electrical stimulation, by passive movement and massage, or by rest. They wish to emphasize that these findings deal only with the amount of atrophy Studies are now in progress with a view toward establishing the status of the treated muscles, as to their histologic structure, the amount of degeneration and the degree of regeneration

The effects of massage and passive movement therapy upon regeneration of paralyzed muscles was studied experimentally by the authors in the following experiment Two groups of animals (macaca rhesus monkeys) were subnected to unilateral section of the sciatic nerve These nerves were immediately sutured to assure good alignment for regeneration After a rest period of four weeks, during which time splintage of the paralyzed muscles was accomplished by immobilization in a plaster case (the muscles kept relaxed by flexion at the knee and plantar flexion at the ankle), one group received daily massage and passive movement therapy, the other group of animals was kept at complete rest by immobilization After a period of time, varying from two months in some animals to six months in others, the muscles were examined

The marked recovery of muscle weight in those animals treated by massage and passive movement as compared with those given complete and prolonged rest is well demonstrated. In addition to this quantitative effect, the muscles which were kept at rest showed extreme fibrosis and tendency to contracture. Fibrosis of the joints also was marked. The massaged muscles, however, were supple and elastic and there was considerably less fibrosis and adhesions than in the muscles which were immobilized.

Rest as a Therapeutic Procedure in the Treatment of Flaccid Paralysis—Rest has taken its place as a definite therapeutic procedure in the armamentarium of the physical therapist Recognizing the prompt alterations in the structure of skeletal muscle following damage to its nerve supply, most clinicians favor rest during the early stage This does not mean to of paralysis leave the paralyzed muscles alone. Rest must be accomplished in such a manner as to avoid stretching the denervated muscle. Stretching of such a muscle may result in irreparable damage Splintage, therefore, is indicated in order to prevent this complication

The studies of Chor and Beard have shown that atrophy and degeneration of muscle fibers result from damage to the neural portion of the motor apparatus These changes in muscle are as inevitable as those changes which occur in the peripheral portion of a severed or damaged nerve We need not anticipate that a mechanical procedure is going to check this natural process. We have seen, furthermore, that atrophy is not the all important feature of the lower motor neurone type of paralysis Fibrosis is the chief factor which determines the fate of denervated muscle The invasion of any organ by excess of fibrous tissue results in cirrhosis, and eventually damage to the remaining parenchyma as muscle regenerates by outgrowth from the remaining healthy muscle cells, the importance of preserving the parenchyma is obvious

What we wish to accomplish by treatment is to maintain the muscles in the best state of nutrition and vitality so that when regeneration of the nerve occurs the restoration of the muscle which follows will be at a maximum. This can be accomplished best by (1) encouraging good circulation of blood

and lymph to keep nutrition at its best and to carry off the waste products of dysfunction, and (2) by keeping at a minimum the fibrosis, which soon follows atrophy and degeneration. In the early stage of paralysis rest is indicated with splintage of the weakened muscles to prevent stretching As soon as possible, however, light massage should be started to promote adequate circulation In the later stage, when fibrosis is beginning to occur, passive movement and massage and electrical stimulation should be utilized. The beneficial effects of passive movement and massage in preventing fibrosis and contractures have been conclusively demonstrated The worth of electrical stimulation, however, is in need of further investigation

Posture or Body Mechanics

The importance of good posture or body mechanics was considered in the Medical Cyclopedia, Volume IX, page 1138

The postural syndrome related to obesity leading to postural emphysema and cardiorespiratory failure is discussed by Kerr and Lagen ¹⁰ They believe this is one of the most important syndromes seen in the practice of adult medicine, and they suggest measures for symptomatic relief based upon knowledge of bodily mechanics and function. These authors refer especially to a type of obesity which appears to be exogenous in origin, arising in persons whose dietary habits lead to a caloric intake beyond their daily requirements.

In the fourth decade the appearance of the individual is one of increasing corpulency, with a tendency toward a florid complexion. The normal curves of the spine are accentuated. The added weight of fat of the abdominal wall and viscera moves the line of gravity forward, and to compensate for this the

major portion of the thorax is moved backward, accentuating the lumbar curve. The upper part of the thorax and shoulder-girdle move forward, increasing the normal thoracic curve, and the head and neck are thrust forward as is required for adjustment at a new line of gravity

The fifth decade marks the period of transition from the state of physical well-being and activity of youth to one of gradual lessening of activity of middle and old age There frequently occurs at this time a change in the habits of living, distinguished chiefly by diminution of active exercise or even normal activity, and by increase in the consumption of food Finally, it is at this time of life that changes occur in the body which herald the onset of presentle degenera-These are the depositions of fat, increased flabbiness of muscles, atheromatous changes in the blood vessels and those gradual changes in skin, connective and glandular tissue which are difficult to define These latter may be described as loss of elasticity and repairability with consequent lessened tone and poor response to injury such as strain in muscles and ligaments or pressure on bone and cartilage The syndrome itself is certainly modified or delayed in susceptible individuals by proper exercise and diet

Equilibrium maintained by the body in an upright or standing position is active and not passive, and muscular forces must constantly be engaged in opposing and neutralizing gravitational forces

Viewed from a frontal plane, the line of gravity bisects the body into two symmetrical halves. Viewed laterally, the line of gravity arises, according to Kerr and Lagen, from the supporting surface of the feet between ball and heel, passes through the ankle- and knee-joints, runs between the hip-joint and

sacrum and through the upper ventral portion of the sacro-iliac junction; then runs upward behind the bodies of the lumbar spine, intersects the spine at the lumbothoracic junction, runs slightly in front of the thoracic spine, intersects the spine again at the cervicothoracic junction, runs slightly behind the cervical vertebrae, and touches the head behind the ear at the mastoid process

The postural syndrome has as its basis obesity, which results in the development of a heavy dependent abdomen It is this latter which is the obvious cause of the train of symptoms and signs that ensues Their production depends upon two factors, unrelated except for cause, but synergic in effect. The first of these is the dragging effect exerted by the increased abdominal weight. This makes itself felt chiefly in the lumbar spine to which the weight is transmitted through muscle, fascia and skin Here the result is at first an exaggeration of the normal lumbar curve, later an increasing lordosis with the vertebrae parting ventrally like the leaves in a book. The spine being intimately associated throughout its length, must compensate for this, which it does by causing a thoracic kyphosis and a cervical lordosis sacrum, normally at an angle of 45° to 60° with the lumbar spine, is elevated to an angle of 90° or more

The second factor is concerned with the shift in the center of gravity produced by the excess weight which, as it were, has been attached to the front of the body. This is at first compensated for by increased plantar flexion. When this is no longer effective, the individual is forced to compensate further, which he does by bending his knees and voluntarily increasing the lumbar lordosis through muscular action, the latter resulting also in an effect on the rest of the spine.

This accentuation of the curves, coupled with the bending of the knees, causes a reduction of stature. The increase in cervical lordosis forces the individual to carry his head bent forward, the degree depending upon the lordosis. To maintain the head in the normal position puts extra work on the extensor muscles of the back of the neck, so a position of comfort unconsciously results in the bowing of the head. Hypertrophic arthritis of the spine may be initiated, or exacerbated if already present

The increased thoracic kyphosis is perhaps the most important effect of all in view of the result it has on respiration It results in elevation of the ribs, producing thereby the barrel-chest seen typically in obstructive emphysema, but in this instance without marked emphysematous changes in the lungs This flaring of the rib-cage also directs the lower ribs downward, which with the widening, flattens the diaphragm. These individuals are able to breathe with a great deal more facility when lying flat, since the relief from abdominal weight in the prone position must release the diaphragm They suffer, not from orthopnea, but from orthostatic dyspnea

The reduction in pulmonary ventilation, leading to oxygen-debt on exertion particularly, results in dyspnea This, as stated before, is orthostatic, occurring only in the upright position, but is not present on sitting or in the prone posi-There is a compensation taking place, however, which is the occurrence of polycythemia in the advanced stages of the syndrome, brought on by the reduced oxygenation of the blood often produces some cyanosis, or accentuates that already present effects are on diminution of cardiac reserve from overstrain, constituting, in its effects on tissue-oxygenation, somewhat of a vicious cycle Coincident arteriosclerosis complicates the clinical picture.

In the treatment of their patients, mostly males in the fifth and sixth decades, most of whom have appeared in the later stages of the syndrome, the authors have been confronted with symptoms of marked severity However, those with less marked symptoms have responded well to the same measures. The point of attack is in three directions, but with the same end in view

- 1 Temporary elastic support of the pendulous abdomen
 - 2 Reduction in weight
 - 3 Postural exercises.
- The authors believe that if the patient could be given an abdominal support to overcome some of the weight applied to the diaphragm during inspiration and to relieve the counterweight during expiration, the tidal air would be greatly increased, the spinal curves would be straightened, and the line of gravity moved backward. If a belt were devised which gave abdominal support and if elastic materials were inserted in the belt at the sides of the abdomen, the tidal air could be further enhanced These elastic materials would in effect serve as a method of giving the patient artificial respiration by assisting in the expulsion of gases from the lungs The description of this belt is given
- 2 Reduction in Weight—The plan for reduction in weight must be individualized for each patient, depending upon occupation, opportunity for exercise and general physical condition. A caloric intake should be determined which may be as low as 800 to 1000 calories for some patients. At first two or three pounds per week may be lost and later not more than one or two pounds per week until the patient approaches the ideal weight after a period of six months. In some of these patients the problem of

dietary intake is a difficult one, as all who have treated obesity can test.fy

3 Postural Exercises—Chief among the postural exercises are those which educate the patient to stand properly until the postural reflexes assume com-This requires attention toward the correction of the position of relaxation Patients should periodically stand with their backs to the wall touching the wall at as many points as possible When some of the excess weight has been removed, the abdominal muscles may be strengthened by graduated exercises The familiar admonition to "suck up the guts" employed by instructors in physical education may be very easy to accomplish by boys in their early years, but is almost impossible for the obese

In a Hunterian Lecture on postural deformities of the anteroposterior curves of the spine, Wiles¹¹ states that a permanent change in habitual posture is not maintained by the muscles on one side of the joints concerned contracting more strongly whilst those on the other side are more relaxed This process only causes the movement by which the new posture is reached Once it is reached, all that is necessary to maintain it is a change in the length at which the muscles must remain, and the power required may be no greater than before To keep the muscles habitually at this changed length is obviously a function of the central nervous system and involves the conditioning of a new reflex which regards a new muscle length as normal

The requirements for a good posture in an otherwise healthy body are adequate muscles and correctly conditioned reflexes. The muscular power required to maintain posture is so small that it is unusual for muscular weakness alone to be the cause of postural deficiency. In a large proportion of cases the error

lies in the postural reflexes, and it is to this that attention has chiefly to be directed

The causes which lead to the development of faulty postural reflexes, or to a change from good to faulty reflexes, are little understood. A great number of postural deformities commence in late childhood and adolescence, during periods of rapid growth. There are many ways in which this can be brought about, at the present time a common one is undernutrition. Toxaemia from some chronic infection is another factor which may play its part, and one which is itself greatly aggravated by undernutrition.

Wiles believes that sometimes, however, it does seem possible to make a direct correlation between the psychopathological findings and the physical condition, and certain cases of postural deformity provide excellent examples

Since it is impracticable to measure the spinal curves directly, attention has been turned to an indirect method The spine is attached to the pelvis at the lumbosacral junction, so that any movement of the pelvis will cause a corresponding movement of the fifth lumbar The habitual posture of the pelvis therefore determines that of the fifth lumbar vertebra, which in turn must affect the posture of the whole Hence measurement of lumbar spine the inclination of the pelvis should give an estimation of the curve of the lumbar spine

Wiles has devised a simple method of measuring the pelvic inclination, which he believes is of sufficient accuracy. Measurements of the inclination of a fixed object give readings accurate to 1° with different observers. Repeated measurements of the pelvis of the same people on different occasions gave a variation of + or - 2° . This wider variation is accounted for by a slight

difference in posture on the different occasions, and it is not present if the person stands still whilst several observations are made

The instrument consists essentially of a pair of external calipers with a vertical plate fixed at the hinged end in such a way that it is always in a plane at right angles to the plane of bisection of the calipers. The plate is graduated in degrees, and a plumb-line suspended so that the inclination to the horizontal can be read directly from the scale.

The points taken for measurement are the upper border of the symphysis pubis in front, and the level of the posterior-superior spines behind. This posterior level was chosen, rather than the fifth lumbar spine, because the latter is much broader and often difficult to palpate accurately.

Wiles in a series of examinations found 56 per cent of the men and 46 per cent of the women to have normal curves and normal posture. The pelvic inclination in the men ranged from 34° to 26°, with an average of 31°, and in the women from 33° to 23°, average 29°

Wiles in an analysis of muscular control concludes that the inclination of the pelvis is controlled almost entirely by the muscles surrounding the hip-joints. The abdominal and spinal muscles have little direct effect on the pelvis, their action is to keep the body upright, whatever the pelvic inclination, by varying the curves of the spine

It is essential for the maintenance of the upright position, whatever abnormality of posture may be present, that the center of gravity of the whole body should fall somewhere within the area occupied by the feet. This limits considerably the possibilities of postural variation, and analysis shows, according to Wiles, that only two components contribute to make up the majority of cases

Firstly, there is nearly always an alteration in the pelvic inclination, which may be increased or decreased Secondly, there may, in addition, be a dorsolumbar kyphosis. These two variables combine to produce four distinct groups which are adequate to classify the majority of cases. (In the following, "normal spine" means one which has no intrinsic error and whose curves become normal when the pelvic inclination is corrected.)

Forward tilt normal spine lumbar lordosis of pelvis plus dorsolumbar kyphosis sway back

Backward tilt normal spine flat back of pelvis plus dorsolumbar kyphosis round back

Treatment—Before embarking on the treatment of postural deformity, inquiry should always be made into its cause. To give remedial exercises to an undernourished patient is only adding to his troubles. When no other cause is forth-coming, investigation should be made into possible psychological factors.

Wiles believes that the treatment of postural deformities falls into three stages. Firstly, restoring sufficient mobility to enable correction to be made, secondly, acquiring voluntary control over the movements that produce correction, and thirdly, the establishment of new reflexes that will maintain permanently the correct posture. Any good system of remedial work deals with all three stages simultaneously, they are only separated here for discussion

- 1 Mobility—There are three causes of the loss of mobility, one or more of which may be present in any case
- (a) A structural change in the shape of the bones. It is doubtful if any of the most drastic corrective machinery used by orthopaedic surgeons has any effect on it
- (b) Contracted ligaments The stretching of contracted ligaments, as of any

other fibrous tissue, is a matter of difficulty. The most effective method of stretching them at all rapidly is prolonged traction. Head suspension is therefore very valuable when dealing with contractions affecting the spine, and, if carefully supervised, is well tolerated by patients. Active movements carried to their extreme range and repeated frequently may be of some assistance in stretching ligaments

(c) "Shortened muscles" The process of increasing the length of muscles is often referred to as muscle stretching This is hardly the right word to use because, so far as is known, musclefibers cannot be stretched—they have to be made to relax more fully not merely an academic point, but a practical one which directly affects treatment The normal physiological response of a muscle to stretching is contraction, and the harder it is stretched the more Therefore, passtrongly it contracts sively stretching a muscle calls into action this "stretch reflex" and makes the muscle contract more The passive stretching of muscles with the idea of lengthening them is a procedure that should be abandoned, it can do no good, and, if carried to an extreme, it will do harm

The lengthening of a muscle can be achieved by getting it to relax more fully. A muscle relaxes reflexly when its antagonist contracts, but, when a "free" movement is made—that is, one without any resistance to it—the muscle does not relax completely, it maintains enough tone throughout the movement in order to keep the joint under control. However, when a movement is made against resistance, the muscle is enabled to relax more fully because control of the joint is obtained by means of the pressure between the resistance and the contracting muscle.

muscle, its antagonist must be made to contract against resistance and continue to work against the resistance when the extreme of movement has been reached Thus, if the flexors of the hip are contracted, the appropriate exercise is to extend one leg backwards against gravity whilst keeping the trunk vertical.

2 Voluntary control over the movements that correct a postural deformity is easily taught when adequate mobility is present

In cases where the pelvic inclination is increased, the gluter are the correct muscles to restore it to normal. The gluter are the principal extensors of the hips and tilting backwards the pelvis is exactly the same movement as extending the hips. Patients should not be told to "draw the stomach in" or they will use the abdominals. They should be given some such order as to "tuck their tails under them," and then be watched to see that they really are using the gluter

3 The establishment of new postural reflexes is the final aim of all remedial treatment It is just here that so many systems show their greatest weakness They are mainly concerned with strengthening muscles and increasing mobility, and make little effort to teach the patient how to hold the new posture Remedial work requires "postural fixation" not "postural change," so, when it is possible to make a voluntary correction, exercises that move the parts of the body principally concerned can do no good Exercises must be directed towards keeping those parts as still as possible whilst the rest of the body is moved Thus the patient is taught to keep a good posture during every variety of movement

Wiles emphasizes that it is not movement, but absence of movement, of any given part that is essential for the establishment of a postural reflex

FOOT DISORDERS

The treatment of painful feet was considered in Service Volume XIII, 1936, p. 967 This year some valuable articles on this subject have appeared Graham¹² states that success in the treatment of the common type of weak foot due to poor posture depends upon the intelligent employment by the physician and the patient of five separate but simultaneous lines of attack (1) maintenance of correct posture, (2) proper use of the foot in walking, (3) exercises for the re-education of foot and leg muscles; (4) properly constructed shoes that fit correctly; and (5) a temporary crutch in the form of an arch support

In this discussion the writer has in mind the uncomplicated weak foot

In the common type of postural defect due to poor postural habits, the head is dropped down and forward, the shoulders are dropped, the thoracic kyphosis is increased, the abdominal muscles are relaxed, allowing the abdominal organs to fall down and forward, and the lumbar curvature is accentuated. The center of gravity of the body is shifted forward and the load on the sacrum is consequently moved forward The sacrum as a result rotates about its axis, the pelvis moving with it With this shifting forward of body weight, the line of gravity moves forward and falls in a plane through the anterior borders of the hip sockets The change thus produced in weight distribution of the superstructure necessitates an adjustment in the supporting femoral columns Graham states that this is accomplished by internal rotation of the femurs

Internal rotation of the thigh is reflected in the ankle Rotation at the knee joint is possible only when the knee is flexed. Ankle rotation cannot take place when the foot is perpendicular to

the leg It is obvious then that when the individual assumes the erect position, with the knee joint extended and with the foot held at a right angle to the leg, that the femur, the tibia with its attached fibula, and the astragalus must move as a unit

The effect on the foot of internal rotation of the unit composed of the femur, tibia, and astragalus, is the production of a relative valgus position because the astragalus, rotating internally, moves inward and downward in relation to the calcaneus. The effect on the astragaloforefoot relationship of this movement of the astragalus, about the calcaneus is the same as that of an outward and upward movement of the calcaneus about the astragalus because the calcaneus and forefoot move as a unit. It produces a valgus relation between the forefoot and the astragalus

The valgus relation between the astragalus and the underfoot, the result of faulty posturing of superstructure musculature, disturbs the balance in the foot posturing muscles and it is the strain of the extra load thrown on one group of these muscles that is behind the clinical manifestations of the condition known as weak foot

An individual analysis of the major foot posturing muscles is given by Graham

Diagnosis—Physiological and anatomical diagnoses, Graham believes, are as important in the simple and complicated weak foot as they are in heart disease or biliary tract disease

While the common and, in fact, the usual cause of weak feet is the anteriorly shifted center of gravity of the body resulting from poor postural habits (slouch posture), it must be borne in mind that many other conditions such as anterior poliomyelitis, arthritic disturbances, injuries and structural abnor-

malities may underlie maladaptation of the weight bearing mechanism to the superstructure, and the possibility of the presence of these conditions must be eliminated before the pedal disturbance is laid at the foot of poor posture

Treatment—Treatment, if it is to be successful, must include five separate methods of approach to the pathological physiology here presented and all five of these approaches must be made simultaneously

- 1 Maintenance of Correct Posture—Postural correction in the patient depends firstly, upon instilling into him an adequate conception of correct posture and secondly, upon exercises that will increase the tone of posturing muscles. The exercises outlined by Graham are listed with those for the feet to make one complete set of exercises.
- 2 Correct Use of Foot—If body weight is to be carried efficiently on the longitudinal arch, the crown of the arch and its anterior and posterior supports must be in the same plane. These conditions will be satisfied roughly from the clinical point of view when the inner edge of the second toe, the head of the astragalus and the base of the calcaneus are in the same line, with the foot adducted, that is, pointing straight ahead

In addition to adduction and external astragalar rotation, both supports of the anterior arch, namely, the first and fifth metatarsal heads, must be on the ground A most valuable exercise for teaching the patient to adduct the foot, externally rotate the astragalus and push the first and fifth metatarsal heads into the ground, all at the same time, is the exercise which is given below, known as the "chair maneuver"

The patient sits on a chair with the foot on the ground and with the leg below the knee vertical. His leg is then held just above the ankle by the physi-

cian This prevents leg movement A mark is made on the floor about an inch and a half internal to the first metatarsal head and the patient moves the front part of the foot to the mark. It is important that only the front part of the foot be moved. The big toe is then depressed so that the skin beneath the metatarsal head touches the floor. In practice the patient should place two fingers on the outer side of the lower third of the leg so that he can feel the peroneal muscles contract when he depresses the first metatarsal.

The same principles can be brought out in another maneuver in which the patient walks very slowly across the room steadying the laterally extended arm against the wall The heel is touched to the ground with the foot adducted and the body is moved forward with the weight on the outer side of the foot With the weight still on the outer side of the foot the first metatarsal is depressed and the body rises on the toes with a spring The walking is continued in this manner while the patient concentrates on "heel, outer side of foot, big toe, and spring" This maneuver impresses upon the patient the lever function of the foot

3 Exercises—Patients find that they can run through many of the exercises listed below at odd intervals during the day, and this is advisable. However, the complete set of exercises should be performed twice daily. It is often difficult at first for patients to go through some of these maneuvers barefooted but they should strive to do this as quickly as possible.

Graham gives the following instruction to his patients

Standing

- 1 Head up, shoulders back, abdomen in, pelvis,
 - 2 Feet four inches apart;

- 3 Toes pointing straight ahead,
- 4 Weight on outer edges of feet,
- 5 Arches cupped, like palm of hand

Walking: Take a two mile stretch daily, preferably at noon. This does not include walking while at work. Keep in mind

- 1 Toes pointing straight ahead,
- 2 Weight on outer edges of feet,
- 3 Toes gripping the ground to cup the arches;
- 4 Keep conscious of "heel," "outside of foot," and "big toe and spring"

General.

- 1 When standing, practice gripping ground with toes.
 - 2 When walking, do the same,
- 3 When sitting, cross feet and practice cupping arches

Exercises and Postural Aids—Twice daily, barefoot as soon as possible, and toes always straight ahead Time—six minutes

- 1 Wall maneuver—Begin at wall, walk around room five times, checking posture at wall each time
- 2 Chair maneuver—Depress and elevate the big toe 20 times (each foot)
- 3 Neck rotation with muscles on stretch, five times
- 4 Arms extended forward and backward with deep breathing, ten times
- 5 Touch floor with knees straight, five times
 - 6 Leg raising, lying on back, five times
- 7 Push back into floor and relax alternately, ten times
- 8 Up on toes, cupping arches by throwing weight on smaller toes, ten times
- 9 Up on toes, roll out on sides, and down, ten times
- 10 Feet together, roll out on ankles, ten
- 11 Walk across room on toes, and back on outer sides of feet, three times
 - 12 Manipulate teet as directed, five times
- 4 Proper Shoes—The inner border of the shoe along the first metatarsal should be straight and it should parallel a line perpendicular to the heel base. The front of the shoe should have a wide outward and backward sweep from the tip of the first toe around and behind the fifth toe. The blunt toe does not

necessarily mark a properly designed shoe and it often leads one into buying a shoe that is too narrow

The sole should be flat and fairly flexible.

The heel of a shoe makes walking easier by inclining the body somewhat forward. The heel must be broad Its height may vary from $\frac{3}{4}$ inch in men's shoes to 1 or $\frac{1}{4}$ inches in women's shoes

It is always advisable to have the patient buy shoes on approval so that they may be brought to the physician's office for inspection

5 The Arch Support — The arch support is the factor of least importance in the treatment of the uncomplicated weak foot, in the complicated weak foot it plays a very important rôle

It is a temporary measure and it should be used only after the patient fully appreciates that the arch support will not only cure his condition but that it is the factor of least importance in the treatment

When used, the support is worn continuously for from four to six weeks. At the end of this time its use should be tapered down over a period of two to four weeks so that within six to ten weeks from the time of beginning treatment, the patient should have discarded the support

The practice of using factory-made supports, or standard, ready-made forms, is likewise a mistake, according to traham. The variations in the size and shape of the pedal arch system cannot be met by ready-made supports.

In a consideration of some factors which influence the balance of the foot in walking, Schwartz and Heath¹³ state that instruments of precision essential to the analysis of gait have been developed. The accumulation of 2500 electrobasographic records reveals the indica-

tion for the presentation of facts relevant to a particular phase of the whole problem of human locomotion. In reality, their present discussion is limited to the stance phase of "normal" gait. This phase of gait is defined as the time interval between the placing of the heel and the lifting of the great toe from the floor

It is agreed that pronation, variable in degree, may exist in such a weight-bearing foot. Moreover, it is common to observe local and referred symptoms in association with such pronation. The converse is also true, ie, these characteristic symptoms almost never prevail in the absence of pronation. It must be stated with emphasis, however, that some pronated feet are not painful

In the order of normal weight-bearing, the foot has two divisions—the heel and the midfoot. The forefoot is a mechanism essential to propulsion of the body, its weight-bearing function is secondary.

It has been conclusively demonstrated these authors believe, that normal foot contours are not retained by virtue of the shape of the bones and of the strength of the connecting ligamentous capsules. These demonstrations prove most conclusively that the opposite statement is true. When the bones of the foot and the leg are joined only by their ligamentous capsules, their relationship is distorted in the weaker position of pronation when downward pressure is applied to the tibia.

Both intrinsic and extrinsic muscles with their respective tendons are the essential structures upon which the foot is completely dependent for balance in walking. Of these two, the extrinsic group has the predominant influence

The posterior group—the peronei and the tibialis posterior, which initiate plantar flexion, and the gastrocnemius and soleus, which lift the body weight—does the most work in normal walking

The antagonistic anterior group of muscles is much weaker The gastrocnemius, in relation to its origin and insertion, frequently precludes the possibility of avoiding pronation when the subject walks without elevation of the heels. Moreover, the relationship of the tendo achillis to pronation becomes of particular importance because of the disparity in alignment between the os calcis and the The muscles which control the medial and lateral aspects of the foot can never prevent pronation in the presence of these two causes—malalignment of the weight-bearing axis of the os calcis, and "contracture" of the tendo achillis

These extrinsic muscles of the leg send to the foot their strong tendons Structurally, they are arranged to form a tendinous sling in which the bones of the foot are suspended. In fact, this is the only mechanism upon which the foot can depend for protection against the development of abnormal contours The disparity in alignment between the weightbearing axis of the tibia and the os calcis is a primary cause of pronation The ligamentous capsules of the joints, particularly of the calcaneoscaphoid joint, cannot prevent the development of this or of any other abnormal relationship between the bones The extrinsic muscles of the foot, through their tendons which suspend the bones of the foot, can prevent pronation only when their functional balance is efficient in counteracting the malrelationship normally existing between the tibia and the os calcis, and the other factors which favor instability

The electrobasographic records reduce the intricate and complex functional interrelationships to a common denominator, previously defined in terms of time intervals. These apply to each foot and are obtained while the subject walks at a natural, uninstructed rate

Early in the work, it became apparent that balance of the foot was greatly influenced by the character of the shoes worn by the subject

In many instances, shoes, made without regard for the natural and essential balance of the "normal" foot in walking, produce adverse influences beyond the natural power of compensation for their presence.

Electrobasographic records were made on normal girls entering the nurses' training school at the average age of 19 years, while the subjects were wearing their own street shoes which they had brought from different cities. These shoes gave a fair average of conventional shoe design. Pronation was present in each case when street shoes of conventional design were worn. It was absent when the subjects wore shoes made to provide for balance of foot function in the stance phase of the step.

The treatment of pronation, therefore, requires that consideration be given to the foot and the leg as a unit. Only through shoes which provide balance for the foot in the stance phase of gait can we compensate for malignment of the os calcis with the tibia and the common contractures expressed through the tendo achillis

The two most common external signs of foot disorder according to Morton¹⁴ are (1) a pronated, unbalanced posture and (2) callus formation on the sole of the foot, behind the second and third toes Pronation occurs usually as "weak ankles" early in child life. Its long recognized association with trouble in the longitudinal arch has not only made it the best known sign of foot disorder but has established it also as a morphologic index by which the degree of trouble is estimated. Callus formation in the area designated is likewise typical

of foot disorder but, since it does not develop as a rule until after physical maturity (25 years or more) has been attained, its significance is not so generally recognized. The author believes that both of these signs point directly to a functional deficiency in the first metatarsal segment.

Two structural conditions have been identified by Morton which are directly responsible for the impaired functional qualities of the first metatarsal segment. They are (1) laxity of its plantar ligaments, allowing a dorsal hypermobility which prevents the first metatarsal from attaining firm supporting contact with the ground at the same time as the others and (2) shortness of the first metatarsal bone, whereby the more advanced head of the second metatarsal must serve alone as the fulcrum of the foot's leverage action

Laxity of ligaments in the first metatarsal segment affects both distribution of weight and postural security. The double burden it normally supports in stance falls on the second metatarsal in the same way as when five men are carrying a heavy log and the man on the end lets go his hold—his share falls immediately on the man next to him. Also, through the relative noncontact of the first metatarsal, the medial margin of structural security is primarily reduced to the short distance between the normal axis of balance and the head of the second metatarsal

The overloading of this more slenderly built bone causes its ligaments to be strained and stretched, and the foot pronates or rolls mediad. If the hypermobility of the first metatarsal segment is slight, ground contact is quickly gained and the movement is arrested, but with modifications in function which characterize what may be designated first degree pronation. Morton then shows

the effects produced by a more advanced degree of hypermobility

Shortness of the first metatarsal impairs the effectiveness of the first metatarsal segment chiefly in locomotion, because the more advanced position of the head of the second metatarsal causes the latter to act alone as the fulcrum of the foot's leverage When the heel is raised in locomotor effort, all the stresses must converge on, and be transmitted by, this more slender bone. The condition is an inherited one and its presence from birth causes the shaft of the second metatarsal to become increasingly hypertrophied throughout the physically active periods of life. The widening of its shaft results apparently from the convergence and crossing of the two streams of locomotor stresses, the thickening of the walls (cortex) seems due more directly to the exaggerated vertical stresses

A short first metatarsal bone affects chiefly the basal joints of the second metatarsal segment by reason of the intensified breaking strains imposed on the latter's plantar ligaments. These strains, acting as repeated injury, produce a local inflammatory reaction of the midtarsal joints, which becomes gradually an actual traumatic arthritis, accompanied at times by an effusion tending to separate the bones.

A short first metatarsal bone forms a very unfavorable combination with the high heeled shoes of women

Morton believes that ordinary disorders of the foot are not difficult to treat and respond readily to a thoughtful and methodical plan of procedure. The important objective to be borne in mind is first to restore a painless condition and then to establish improved conditions of function. This demands equal attention to three clearly defined sources of pain and disability, namely, (1) superficial irritation, (2) deep trauma and in-

flammatory changes, and (3) disordered mechanics

1 Superficial Irritation—The first step in treatment applies to all surface elements of discomfort Painful calluses, corns, warts or other skin growths should be regarded as foreign bodies Patients will not recognize success in treatment of foot disorders as long as they continue to experience discomfort from these superficial sources The manner of treating them, whether through the services of a chiropodist or by means of x-rays, radium, electricity or chemical preparations, is best determined by the nature of the growth After their removal, the area should be protected with adhesive tape or moleskin for a period of a month or six weeks

It is equally necessary to check immediately on the style and fitting of the shoes, especially the shoes that are worn during working hours

2 Deep Trauma and Inflammatory Changes—Too frequently an immediate cure is expected from the mere application of some mechanical device to the foot or shoe. Sick people are put to bed, strained joints in other parts of the body are immobilized and treated locally, but strained feet are expected to get well while they continue their usual daily labors. Thus it is not always easy to obtain full co-operation of the patient.

Emphasis must be placed on the fact, therefore, that all reasonable restriction of physical activities is imperative during the painful period. In addition, a brief interval of reclining or sitting with the feet elevated to hip height should be arranged for the morning and afternoon in order to minimize the cumulative irritation of continued function.

Circulatory stimulation is the most effectual means of combating muscular exhaustion, trauma of the tissues and in-

flammation, and also the various forms of nerve and vasomotor disturbance. Different forms of physical therapy are used for this purpose, but contrast plunges deserve special mention because of their high degree of effectiveness while entailing little or no expense to the patient. They are taken in two buckets with the water of sufficient depth to submerge the feet and legs at least 6 inches (15 cm.) above the ankles. The timing is important

The feet are plunged first into hot water as hot as can be borne comfortably for one and one-half minutes and then immediately into the cold water for one-half minute. After repeating the process five times, the feet are dried by a brisk rub with a rough towel This treatment should be followed by a half hour of reclining, during which light exercise of the toes and ankles is recommended in order to maintain the circu-Contrast plunges latory stimulation. should be taken once a day and preferably as soon after working hours as possible

Special exercises are useful after subjective symptoms have subsided, before then exercises in which body weight is borne on the feet may do more harm than good

3 Disordered Mechanics — It has been shown that disorder in the longitudinal arch and also in the metatarsal portion of the foot originates as a functional deficiency of the first metatarsal, through either laxity of ligaments or shortness, this member lacks the necessary supporting contact with the ground However, while that contact cannot be gained by the bone, it can be accomplished by raising the supporting surface beneath its head

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a small platform which is located under the head of the first metatarsal. Since the proper height of the platform can be determined only by trial, an insole permits easy removal for any necessary adjustments, while it maintains the platform securely in position when in use. This method makes no attempt to supply an artificial support which acts by assuming the weight stress that should normally be borne by the structure of the foot. It operates by creating a more natural distribution of the stress to every segment of the foot

The second method, which is especially useful in children, employs a light piece of flexible metal covered with leather, whose base is located under the heel, and having an extension carried upward on the inner side of the foot to the region of the navicular bone. Body weight imposed on the heel is thus utilized through the extended portion to offer resistance to any tendency of the foot to roll into a pronated posture. As a result stresses that would otherwise become concentrated on the second metatarsal are distributed on all four of the lateral metatarsals.

ERYSIPELAS

Ultraviolet Radiation — Attention was directed to the value of ultraviolet radiation in the treatment of erysipelas in Service volume XIII, 1936, p 978 and XIII, 1937, p 962.

The statistics for erysipelas in infancy according to White¹⁵ show a high mortality rate for those two years of age and under varying from 45 to 26 per cent, depending on the age of the patients. Those under six months old show a mortality rate as high as 70 per cent, the figure falling to about 20 per cent for age of two years. The statistics for the Isolation Hospital, Windsor, for

infants two years of age and under were 71 per cent, and for infants under six months of age 20 per cent. The highest mortality occurs where the infection is in the body, and the lowest where the infection is in the extremities.

A brief synopsis of 13 cases is reported From 1930 to 1932 there was no definite plan of procedure, other than daily lamp treatments Transfusions were given irregularly, and an occasional patient was given some antistreptococcus serum or antitoxin, but in later years transfusions were given early and repeated Lamp treatments were given daily in erythema dosage. No other treatments have been used, other than good general nursing care, with particular attention paid to fluid intake.

White concludes that ultraviolet lamp therapy is a valuable procedure in erysipelas of infancy, and transfusions are a valuable supportive measure. Transfusions should be given as early as possible and repeated in two or three days as required. Erysipelas in young infants need no longer be considered a fatal disease, with energetic treatment one may venture a more favorable prognosis than heretofore

In the treatment of erysipelas by ultraviolet, Bieker¹⁶ states that the aim should be in every case to produce the desired erythema, which is just short of vesiculation, at the first treatment When this is done a second or third exposure is often unnecessary Most patients, when this is satisfactorily explained to them, will gladly submit to the minor after-effects of a severe sunburn without complaint Even a blister, while uncomfortable for a time, is not dangerous If, therefore, there is any question as to the exact dosage, overtreatment rather than undertreatment is to be preferred. If a satisfactory erythema has not developed within twelve hours after the first exposure, treatment may be repeated at this time to produce the desired degree of reaction If, within 24 hours, there has been any extension of the lesion, or if the temperature has not dropped satisfactorily, the dose is repeated, and this is continued at 24-hour intervals for as long as may be deemed necessary A margin of two inches of healthy skin around the lesion is treated and the surrounding area protected by towels or black paper The most virulent portion of the lesion is at the edges In facial cases the eyes are usually protected by a narrow strip of wet cotton along the margin of the lids

To the cases already on record the author adds a report of 20 cases these nine were facial, four had involvement of the arm, six of the leg, and one the back of the neck number of treatments averaged two and one-third No case was included in which there was any doubt as to the diagnosis The author's average as to number of treatments was raised considerably by one case in which abscess formation complicated the picture, and by two cases in which the auditory canal was involved In another case there was a recurrence after some weeks, both attacks were controlled with one treatment cases two treatments were given These had marked improvement after the first, and complete cure after the second treatment Altogether, the results have proved highly satisfactory to everyone concerned

Jenkins¹⁷ states that out of 50 consecutive cases of erysipelas treated with ultraviolet, 25 had only one treatment, the temperature returning to normal in two days. Thirteen had two treatments, the temperature returning to normal in an average of 3 84 days. The remainder had three or more treatments. The entire group had an average of 1 9 treatments and the fever returned to normal.

and remained so in an average of 3.13 days. Nineteen had temperature from 103 to 105° F. (394 to 405° C.) with a leukocyte count ranging from 10,000 to 39,500, and average of 15,000. Fifteen had a temperature of 101 to 103° F (38.3 to 394° C.) with the average leukocyte count of 11,000. Fifteen had a temperature of 100 to 101° F (378 to 383° C) and one 998° F. (37.6° C)

Of the 50 patients one died, giving a mortality rate of two per cent. This was an infant 20 days old. The patient entered the hospital with a temperature of 104° F. (40° C) with involvement of the lower portion of the abdomen, both thighs, and one leg and foot.

In the summary the author states that ultraviolet radiation for erysipelas has proved superior to other remedies, and that the mortality rate is lower than that of any of the other methods of therapy

The ideal treatment of erysipelas as given by Fox¹⁸ is a combination of serum, the ultraviolet ray, and Burow's solution. Serum is not necessary in mild or moderate cases and its use is therefore wasteful

The hospital records of the author show that the serum-treated cases have the longest stay in the hospital. The use of the antitoxin seemed beneficial only in the severe type of erysipelas Added to the antitoxin were the ultraviolet treatment and local application of Burow's solution It is the opinion of the author that mild cases need only have local application of Burow's solution, that the moderately severe cases may be treated with ultraviolet and Burow's solution In severe infection with high fever, bleb formation, and rapidly spreading lymphangitis, the triad of serum, Burow's solution and ultraviolet rays gives the best results

Two years ago Knapp reported 340 cases of erysipelas treated by ultraviolet

radiation alone The present report by Knapp¹⁹ brings the study through the year of 1936

During 1935 and 1936 there have been treated 116 cases of erysipelas Of these, 91 were treated by ultraviolet radiation alone

The technic consisted in exposing the involved area and a margin of one to three inches of normal skin to ultraviolet radiation. In facial erysipelas the eyelids were left uncovered if they were involved, otherwise, the eyeballs were covered with small circles of paper, leaving the eyebrows exposed.

Erysipelas has long been known as an extremely fatal disease in small children. The mortality rate has usually been reported at 50 to 75 per cent with the older methods of treatment. In this series, there were nine children whose ages were three years, two years, 1½ years, 16 months, one year, 9 months, 4½ months, and two at one month. Only one of these died. To this group the author can add three private cases under one year of age without a death.

From 1929 through 1936, all four series, had 18 children under one year of age with only two deaths of 111 per cent. This Knapp believes is a remarkably good record.

In conclusion the author states that

- 1 Ninety-one cases of eryspielas treated by ultraviolet alone are added to the previous reports from the Minneapolis General Hospital. This enlarges the entire series to 510 cases.
- 2 Ultraviolet radiation has given consistently good results over a period of eight years
- 3 The complications and deaths are discussed
- 4 Ultraviolet seems to be particularly useful in reducing the mortality among small children.

PELVIC INFLAMMATORY DISEASE

Elliott Treatment - Randall and Krusen²⁰ in considering the Elliott treatment of pelvic inflammatory disease of women state that in this type of treatment a distensible rubber bag is inserted into the vagina The bag is then distended by means of water under controlled conditions of temperature and pressure, in order to apply the heat to as much of the pelvis as is possible The greater the distensibility of the vagina and the greater the amount of distention of the bag, the greater the area that will receive heat, the less the distention, the less the efficiency and value of the treatment, regardless of the amount of temperature that may be applied The amount of actual pressure necessary to accomplish this distention varies with each patient and frequently in the same case at different treatments In some cases it is never possible to obtain sufficient distention to secure proper radiation of heat This form of therapy should not be employed in such cases

The second principle of the treatment consists of the application of heat Here again no universal rule can be made. The ideal temperature is that which can be tolerated at a given distention of the vagina and which will permit the maximal application of heat to the pelvic viscera If these details of temperature and pressure are carefully followed, one has the basis for successful employment of this method. The authors have observed these factors in the application of more than 4000 treatments at The Mayo Clinic and are convinced of the soundness of the statement The average amount of pressure employed by the authors has been 22 pounds and the average temperature of the water has been 127° F (528° C).

Randall and Krusen have for some time treated gonorrheal infections with artificial fever in patients who could tolerate this form of therapy. The results have been satisfactory in more than 85 per cent of cases Elliott treatment as the sole means of employing heat is now used only in those cases in which fever therapy is not tolerated, it virtually always is used in association with the local measures commonly employed The results are inferior to those obtained with fever therapy or the combination of fever therapy and the Elliott treatment In cases in which this combined form of heat therapy is employed the number of treatments seems to be materially reduced when compared to the number required when fever therapy alone is employed When this combined method of treatment is employed, the Elliott bag is inserted into the vagina after the temperature of the patient has reached the level which is to be maintained in the fever cabinet Treatment is then given for one to three hours, at an average temperature of 122° F (50° C) A temperature somewhat lower than that used when the Elliott treatment alone is employed seemed desirable to the authors as the general increase in bodily temperature probably lessens the local dissemination of heat and local damage to the vaginal mucosa might result

One of the principal considerations in the discussion of any form of therapy is the proper selection of patients. For many years it has been an axiom in the treatment of pelvic inflammatory disease of women that no active local treatment should be instituted in the acute stage, with the exception of the drainage of collections of pus. Randall and Krusen believe that, on the whole, this axiom is still true. Exceptions are made in cases of postpartum infections and infections.

which follow abortion, in which the Elliott treatment has seemed to be of benefit

The authors have divided the cases of chronic infection into two groups: Gonorrheal or specific infections, and infections of nonspecific origin. In the former group the patients have all received the usual local medical treatment of the urethra and cervix. in addition to the application of heat to the vagina. The results of the Elliott treatment and topical applications in 45 cases of chronic gonorrheal infection showed 25 patients cured, ten with residual evidence but negative cultures, five no improvement and five with incomplete treatment. One hundred and seventy-three patients who had chronic pelvic inflammatory disease of nonspecific bacterial origin were treated by the application of heat to the vagina Of this number, 46 required surgical treatment, ten showed no improvement, 17 slight, 48 moderate and 52 marked improvement

The general program followed by Randall and Krusen in administering heat by the Elliott method is to give the patient as much treatment per day as can be tolerated and to repeat the treatment daily for about seven days. The duration of the daily treatment will vary from one to three hours, either in intervals or as one continuous procedure. In a small number of cases the treatment has been continued as long as six hours. At the end of a week the pelvis should be re-examined and the findings compared to those present before the treatment was instituted.

The authors believe that this is a very useful method of administering heat to the pelvic viscera of women Properly employed, it will accomplish that which may be expected of heat, namely, an increase in the amount of blood delivered

to the affected part. This is often sufficient to accomplish a cure

A consecutive series of 100 cases of pelvis inflammatory and allied diseases are reported by Lucas 21 In these cases the principal treatment besides time and rest consisted in the use of prolonged heat by the Elliott technic. A total of 2,008 treatments were given with an average of 20 treatments for each case In 64 per cent of cases the results were considered excellent and these cases were discharged as clinically cured Twentythree per cent were discharged completely relieved of subjective symptoms and thus avoided major surgical treatment Thus in 87 per cent of cases the results from Elliott treatments alone were satisfactory Eleven per cent of cases were improved by heat treatments which permitted less radical surgery than would have been possible otherwise Two per cent of cases showed no improvement

Lucas believes that the Elliott technic is an effective and safe method of applying prolonged heat to the pelvic organs, and when surgery is necessary, the preoperative use of Elliott treatments reduces the extent of operative interference and thereby conserves tissue

Some efforts of the Elliott treatment heating were investigated by quantitative methods in the dog by Schmidt and his co-workers 22 Total venous blood flow from various levels of the gastro-intestinal tract was measured over a two and one-half hour period. Heat applied during the second and third 30-minute intervals increased the blood flow from two to four times, under optimum conditions Mucous membranes can tolerate temperatures that would be definitely injurious to the skin, this is made possible by an active hyperemia of such magnitude that the heat is readily dissipated Temperatures of about 1256° F (52°

C.) applied locally to mucous membranes stimulated secretory activity considerably. Lymph formation was not altered until temperatures high enough to produce injury were employed

Because such good results were obtained by the Elliott treatment in female pelvic infections Riba²³ felt that this method merited a trial in the treatment of prostatic disorders. A distensible rubber bag inserted into the rectum and attached to the Elliott machine was the treatment used in these cases. Sixtyseven were clinic and 15 were private patients. The majority of the former were chronic infections, while the latter were acute.

The clinic patients comprised a group of cases which had been coming to the clinic for a period of one to five years. Their treatments had consisted of massages, sounds, instillations, and other routine measures. Cases were not selected, but for convenience were divided into seven groups.

Group 1 Chronic prostatovesiculitis, 19 cases

Group 2 Chronic prostatovesiculitis with multiple arthritis, 16 cases

Group 3 Chronic prostatovesiculitis with contracture of vesical neck, four cases

Group 4 Adenoma of the prostate with infection, nine cases

Group 5 Post-resection, eight cases

Group 6 Acute gonorrheal prostatovesiculitis, 18 cases

Group 7 Miscellaneous group, six cases Acute non-specific prostatovesiculitis, two; acute non-specific epididymitis, one, acute urethrocystitis in a female due to the B Flexner, one, and chronic posterior urethritis, two

Technic—A total of 1459 treatments were given to these 82 patients, averaging about 18 treatments per patient. As

far as possible daily treatments were given to clinic patients while one-half of the private patients took only two to three treatments per week Patients were instructed to come in with an empty rectum on the day of their treatments Treatments were given with patients lying on their backs and with thighs flexed To insert the bag, the motor of the machine was started, the suction turned on, and the bag rolled The external sphincter was well greased with vaseline, the bag carefully inserted, and the pressure increased from two and onehalf to three pounds The first treatment was continued for 30 minutes, with subsequent visits of 45 minutes to one hour which were usually well tolerated

The temperature of the water in the machine was varied between 110° and 130° F (433° and 545° C) It was found that temperatures could be increased during each and subsequent treatments, but the temperature was never elevated above 130° F (545° C) A few patients were unable to tolerate a temperature above 125° F (516° C) A thermometer inserted into the rectum beside the bag usually reads 10 to 12 degrees lower than the machine temperature No accidents have occurred The bags were frequently distended before insertion to determine their worthiness Upon completion of the treatment, suction was again applied and the bag carefully withdrawn

The results obtained in Group 1, 19 patients, ages between 23 and 67 years, were as follows Three became asymptomatic, one showed marked improvement, three moderate, and seven slight improvement In Group 2, 16 cases with arthritis, one became asymptomatic, six showed marked improvement, four moderate improvement, and five practically no improvement The cases in Groups 3 and 4 were surgical adenomas and con-

tractures It was noted that 11 patients obtained some amelioration of their symptoms Group 5 consisted of nine resected prostatics who had residual symptoms of infection and retention. Three showed marked improvement, three moderate, and three only slight improvement. In the acute anteroposterior gonorrheal infections (Group 6) the results seemed to be the best. Ten out of 18 patients (59 per cent) became asymptomatic. Nine of this group were private patients who had, in addition, local treatments as seemed warranted. In the miscellaneous group (Group 7), two cases of acute non-specific prostatitis cleared quickly on three and four treatments each Both patients have remained well for four months One case of urethrocysto-pyelonephritis in a three months' pregnant woman, received marked benefit

Summary—Of the 72 patients who were treated and followed, 16 (22 per cent) became asymptomatic, 18 (25 per cent) showed marked improvement, while 21 (30 per cent) gave evidence of moderate improvement, 12 (165 per cent) showed slight improvement, while 15 (21 per cent) seemingly derived no benefit from the treatments After 30 to 90 days there were some recurrences, particularly in Groups 3 and 4

Riba believes that this method of treating infected prostates is equal to the fever therapy (hyperpyrexia) now in vogue without its inherent dangers

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PERIPHERAL VASCULAR DISEASE

By Géza de Takáts, M D

Treatment with Intermittent Venous Hyperemia—The use of passive vascular exercises (alternating suction and pressure) in the treatment of peripheral vascular disease was considered in Service Volume XIII, 1937, p 957

In the beginning of this century, surgical thought was greatly agitated by the writings of Bier1 on venous hyperenna Acute and chronic infections were widely treated by passive hyperenna Little attention was paid at that time to the circulatory effects of venous constriction and to the advantages of alternating venous constriction with While such treatperiods of release ments by intermittent venous constriction were advocated as early as 1913 by Thies, credit should be given to W S Collens and N D Wilensky² for devising an automatic apparatus with which intermittent venous compression of various intensity and duration can be readily produced An analysis of the results obtained from a later publication (J A M A 107 1960, 1936) reveals that the method is not entirely harmless, as the simple venous stasis, when produced

repeatedly without adequate drainage of the stagnating venous blood might readily precipitate gangrene and amputation in limbs suffering from diminished blood flow In addition, the price of the apparatus was prohibitive for the home use of great masses of people For this reason G de Takáts, F K Hick and J Coulter3 inquired into the feasibility of supplying the patient with a simple inexpensive device intended for use in the home

Method of Application

Any blood pressure apparatus can be used to produce intermittent venous hyperemia, but a wide eight-inch cuff, conically shaped to fit the thigh, is pref-The amount of pressure should not exceed the diastolic pressure of the extremity at that level It varies between 90 and 60 millimeters of mercury The optimal pressure must be determined individually for each case After inflation of the cuff, the dorsal veins of the foot become distended and the toes show definite rubor This reaction must take place within one to two minutes. If absent, the cuff-pressure must be raised or there is such a strong vascular spasm present that it must be first released by physical, pharmacologic or surgical means before the treatment is effective.

This vascular spasm is slight or absent in arteriosclerosis or diabetic endarteritis, but may be marked in Buerger's disease and in the spastic vascular conditions manifesting Raynaud's phenomena. tion is normal, this reactive hyperemia completely compensates for the venous stasis and flushes out the peripheral blood from the terminal vascular bed In limbs with arterial occlusions, the period following release is not capable of freeing the extremity from the accumulated venous blood For this reason a third phase was suggested, which

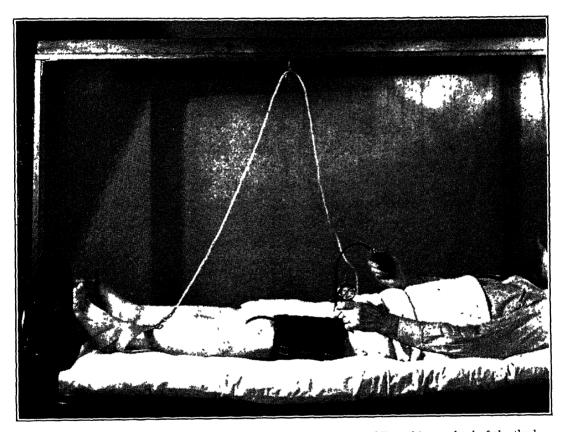


Fig 1—The eight-inch conical cuff is snugly applied to the middle and lower third of the thigh The patient inflates the cuff with the help of a pressure bulb. The gauge can be conveniently hung at a conspicuous place. The leg is elevated with the help of a pulley. For the home, the pulley can be screwed into a door jamb or a wooden frame can be constructed. In milder cases, the patient can actively elevate the leg to the top of four to five firm pillows.

During the period of compression, arterial flow continues but venous outflow is obstructed, thus resulting in a filling and stretching of the venocapillary bed. When the compression is released, there develops an increased arterial inflow, a reactive hyperemia, which often gives the sensation of a warm wave passing toward the periphery. In limbs whose circula-

consists of elevating the leg either actively, by having the patient raise his foot 30° to 40° above the horizontal, or passively with the help of a pulley (Fig 1).

This vascular exercise then consists of three phases one, a period of compression, by inflating the cuff to 60 or 80 millimeters of mercury and obtain-

ing a good rubor of the toes, two, a period of release, still in the horizontal position, which should last as long as the compression did and allows for the development of a reactive hyperemia, and three, a period of elevation, which helps to evacuate the venocapillary bed This latter phase lasts one minute The duration of a cycle is either 1+1+1 minutes or 2+2+1 minutes, and ten cycles constitute one treatment.

It is advisable to have the patient take one treatment in the morning and one treatment in the evening. Most patients are capable and willing to do this exercise at home, but frequent supervision is advisable as changes in pressures or duration of cycles may become necessary. Some patients will not carry on these treatments for any length of time or are too debilitated to do it themselves. In such a case some member of the family may help or an automatic type of apparatus may have to be used. At least 100 treatments are necessary to accomplish any results.

Indications for Treatment—The obliterative type of vascular disease seen in arteriosclerotics, diabetics and late healed stages of Buerger's disease are selected for treatment Pure vasospastic circulatory disturbances seen in Raynaud's disease or Buerger's disease with vascular spasm are not influenced by such treatments. When patients present themselves with mild pain or cramping after walking four to five blocks, but still have a slight pulse in one of the arteries at the ankle, this treatment will be far more beneficial than if they have continuous pain at night, chronic ulcerations or gangrenous digits The stage of the disease in which treatment is begun is of the greatest 1mportance

If venous stasis, edema or ulceration is present, the pressure in the cuff

should not exceed 40 millimeters of mercury. In the presence of a phlebitis, lymphangitis or acute spreading infection, the intermittent venous hyperemia is not permissible. Chronic edema, lymphstasis or a chronic ulceration do not contraindicate treatment, although the method should be used with caution and continuous supervision.

In the presence of marked vascular spasm, the method is ineffective If otherwise indicated, sympathectomy should free the extremity from control or reflectoric vasomotor impulses. For milder forms of vasospasm, heat or vasodilators such as nitrites, papaverine or theobromine can be given concomitantly with the venous compression. In all forms of vasospastic disease, tobacco is strictly forbidden

Results of Treatment - To date over 50 patients, who have had more than 50 treatments each, have been followed Coldness and numbness are the first symptoms which are relieved, intermittent claudication improves slowly, in some cases from a few blocks to three miles, in others hardly perceptibly The degree of improvement depends on the ability of the patient to form collaterals, on his cardiac reserve, extent of damage to the vascular tree, and his mental attitude, which in all these cases is very important Rest pain, if present, is a sign of serious circulatory disturbancy and at this stage little can be expected from such treatments

Comment—In conjunction with other forms of therapy, known to be beneficial for patients suffering from peripheral vascular disease, intermittent venous hyperemia offers a simple inexpensive type of vascular exercise, intended for use in the home, and is available to a larger mass of people, who cannot or will not come to larger hospitals for treatment

with a suction apparatus. In addition, based on some clinical research described in the body of their paper, de Takáts, Hick and Coulter have felt that most of the benefit derived from the suction and pressure treatment is simply produced by alternate constriction and release and that better adaptation of such cycles to the patient's individual circulatory embarrassment will be productive of superior results

There are obvious disadvantages of this method. It requires an active participation of the patient and cannot be used in acute arterial occlusions, where treatments should be almost continuous. In bilateral involvement, the use of double cuffs becomes necessary with simultaneous elevation of the two lower extremities; this may be cumbersome to some patients Finally it may lead to unsupervised self treatment in the home, but this objection is valid for any type of heat, lamp or exercise that may be prescribed for the home

Summary—The simple method described here produces intermittent venous hyperemia combined with postural emptying of the venocapillary bed The compression fills and stretches the vascular tree, the release allows for a chemical vasodilatation to take place in the form of a reactive hyperemia and the elevation empties the terminal vascular bed and makes room for a fresh supply The method should be used in conjunction with other recognized forms of conservative and surgical therapy The general cardiovascular status and its progressive or stationary trend will determine the ultimate result of any local therapy

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PHYSICAL THERAPY IN INJURIES OF ATHLETES

By W H Northway, M D

In a recent article1 attention was directed to the fact that a statistical study of "athletic injuries," especially football, has shown that the most frequent injuries are those of joints, muscles and bones, and in all these injuries soft tissue has been damaged The same statistical study has shown that the most frequently injured parts of the body are as follows, in order of their frequency (1) knee, (2) ankle, (3) shoulder, (4) leg, (5) thigh, (6) hand, (7) head, (8) chest and ribs, (9) hips and pelvis, (10) nose, (11) acromio-clavicular joint, (12) back, (13) foot, and (14) neck Clay Ray Murray² states that physical therapy measures have proven of value in the treatment of soft tissue injuries, therefore, these procedures are particularly useful in the treatment of injuries in athletics The pathological changes which take place following injury to soft tissue are constant, but the extent to which the process advances depends upon the degree of trauma and the early treatment. If treatment is to be carried out on a scientific basis, the pathological changes must be understood by the therapist

In the article quoted above Murray believes trauma to soft tissue results in torn and thrombosed blood vessels, lacerated tissues infiltrated by hemorrhage, inflammatory exudate with its cellular constituents, and the transudate of edema from circulatory and lymphatic obstruction. George O Berg in the discussion of an article³ has described the pathological process which occurs when a muscle is injured experimentally in dogs. The injury corresponds to the so-called "charley horse" of athletes. This experimental work was done some ten years ago at the University of Wisconsin by Dr. Berg. With the above picture in mind, physical therapy can be instituted in a logical manner.

The physical therapy procedures found most useful during the past six years at Stanford University in the department set up for the care of injuries to athletes, under the direction of Dr E F Roth and the author, are simple to carry out and the equipment is inexpensive. The procedures in general have two main purposes to fulfill, namely, prevention of further extension of the pathological process initiated by the original trauma, and to aid in the return of the traumatised tissue to its normal state and function as soon as possible

As the pathological process develops, swelling of the soft tissue takes place, followed by pain and muscle spasm If the swelling in the tissue is allowed to continue, the pressure of the fluid in the intercellular spaces is finally increased to the point where further extravasation ceases This pressure, while it serves a useful purpose in finally limiting the amount of swelling which can occur, will at the same time, if allowed to progress to this point, impede the return of a good blood supply so necessary in the healing process If the exuding of fluid into tissue spaces is to be prevented, it seems only logical that the blood and lymph supply to the part be temporarily diminished, and this can be accomplished in two ways, either by pressure or a lowering of the local tem-

perature, or better by the use of both. Pressure is most conveniently applied by the use of one of the several commercial elastic bandages now on the market. These bandages get their elasticity from the weave rather than the material from which they are made. The initial cost of the bandage is high, but it stands washing well and can be used over and over again The temperature may be lowered by the use of cold or ice compresses, or baths The length of time during which these two procedures should be carried on will depend upon the degree of injury, and no definite period can be prescribed. If the treatment fulfills its purpose, it must be continued until the extravasation of fluid has ceased

During the time that pressure and cold are being applied, another procedure must be instituted, that is, rest to the injured part. Rest may be secured by placing the part in a relaxed, protected position or it may be necessary after the initial application of pressure, cold and rest, to continue the same in bed

Following the arresting of this process of destruction brought about by the trauma, it is necessary to direct the therapy in ways which will aid nature in bringing about repair as rapidly and with as little permanent change in the tissue as possible The fluid and cellular debris which is occupying the intercellular spaces must be absorbed into the blood and lymph channels before it becomes organized into fibrous tissue and before it destroys the surrounding tissue cells through its pressure, diminishing their blood supply The next job, therefore, is the application of measures which will increase the blood supply.

Clay Ray Murray in the article referred to above has stressed the fact that physical therapy procedures to be of the greatest value must be started

early, hours rather than days after the injury, for organization of the exudate begins at an early date. E F Roth⁴ has also stressed this point and believes it responsible for the good results usually seen in the treatment of injuries of athletes The methods used in increasing the blood supply are heat, massage, exercise and elevation of the part. Heat may be applied by several methods, such as compresses, baths, radiant heat and medical diathermy A very satisfactory method, if the anatomical position of the injury will allow, and if a fracture is not present, is the use of the whirlpool bath A whirlpool bath consists of a metal tank into which water is run continuously and in such a manner as to produce a constant motion of the water in the tank The temperature of the water can be regulated by simply increasing or decreasing the proportion of hot to cold water-no complicated mixing valve is needed A pipe may be added to the intake which will pull air into the water circuit before it enters the whirlpool The addition of air bubbles into the bath enhances the value of the heat by producing a soothing sensation on the skin surface, the motion of the water acts as gentle massage, both aiding in the relaxation of spastic muscles The method also allows early active motion with a minimum of work for the muscles Plans for the construction of such a bath may be secured from the Council on Physical Therapy of the American Medical Association

Radiant heat may be secured from two sources, depending upon the penetration desired Experimental work has shown that with radiant energy from an incandescent lamp, using maximum skin tolerance as a gauge of dosage, the subdermal temperature at a depth of five-tenths centimeters rose to 1178° F (477° C) while with infra-red radia-

tion from an infra-red generator at the same depth the temperature attained was 107° F. (417° C.). If penetrating heat is desired, incandescent lamps have an advantage over infra-red generators whose radiations are absorbed on the surface, thereby heating the surface to a greater degree than the deeper structure Radiant heat in either form must be carefully supervised or the skin above the damaged soft tissue may be blistered. It will not stand temperature changes of a normal skin probably because of the deficient blood supply.

Medical diathermy is another useful method for applying local heat short wave medical diathermy seems to be the most convenient method for its application John S. Coulter and S L Osborne⁵ measured the temperature of the skin, of the subcutaneous tissue, and of the quadriceps extensor muscle in human subjects before and after twenty-minute clinical applications of short wave medical diathermy concluded from these tests that there was no specificity of heating of the different wave lengths which they employed The cuff, coil, and pad technic was used In another article by the same men⁶ their experience tended to show that the electromagnetic method (coil technic) was by far the most effective method of producing heat in the depths of (See article on short human tissue wave medical diathermy in this issue)

Massage in sprains and allied injuries, according to R C Elmslie⁷ may be begun quite early, but at first it should be gentle and aim simply at getting rid of effusion. Kneading deeply over an injured area is only to increase the effusion. In carrying out massage on an injured limb, he quotes Mennell as saying, "You should first uncork the bottle before you try to empty it." In other words if there is swelling and effusion

around the ankle, the massage should start high up the limb. If medical diathermy is used it should be used for a short period and at low intensity for the first few doses; thereafter the dosage and intensity will depend upon the reaction of the patient.

Sir Morton Smart⁸ believes exercise of soft tissue not accompanied by bone damage should begin early. Exercise increases the circulation to the part, thereby aiding the absorption of intercellular fluid, prevents the binding together of muscle, tendons, and areolar tissue by fibrous tissue, and increases muscle tone, so necessary in the proper functioning of joints dependent upon the adjacent musculature. Exercise in a damaged muscle should begin with a minimum load.

This may be accomplished by submerging the part in a pool or Hubbard tank or by placing the limb on a powdered flat surface At our clinic at the Stanford University Medical School we employ a special tank of Monel metal with an overhead crane to facilitate the handling of the patient Plans and specifications for the construction of a simple tank may be secured from the Council on Physical Therapy of the American Medical Association The exercise should be increased as the tolerance to work Muscles of the lower limb increases may be exercised following a sprained ankle by using a firm Gibney adhesive tape support to the ankle, crutches to support the body weight, and then insisting that the muscles of the leg be used through their full range of motion by walking The procedure may also be used for injuries about the knee The exercise must be supervised at first to be sure the leg is being used in a natural manner but without weight bearing

H. T Simon⁹ has stressed the importance of exercise of the quadriceps

femoris muscle group following removal of the semilunar cartilage of the knee It is his plan to allow walking supported by a cane as early as the eighth day post-operative The patient should walk as much as possible and flex the knee on walking Knee flexion should be complete by the second week following the operation Exercise on the stationary bicycle is an aid to knee flexion and climbing steps and inclines is encouraged Muscles about the shoulder may be exercised early either by the use of a powdered board with the patient supine, the Hubbard tank, or with the patient leaning forward from the hips with the injured arm dangling at the side. This latter procedure will allow a greater range of abduction and elevation with less work being performed

It has been recognized for some time by medical men interested in the injuries of athletes that injury to one portion of the body does not prevent strenuous exercise of other parts, especially if the injured part is protected sprained ankle is no contraindication to strenuous exercise of the shoulder, back and trunk muscles Likewise, a dislocated shoulder does not hinder a strenuous workout on the track or gymnasium floor provided body contact with another does not occur General body exercises with an injured part adequately protected keeps up the athlete's tolerance for work, allows him to return to his competitive sport in good condition as soon as his injury has healed, and probably during the period of treatment improves the blood supply to the injured part by keeping the general circulation active

A common fallacy exists in the minds of laymen that injuries sustained by athletes are different and heal differently than those sustained in the ordinary individual. An injury received in an athletic contest is no different from a similar injury received at home, in the office, on the farm, or in a factory. The injury may heal more rapidly if intelligently treated but not differently. The same physiological processes are active in each instance Physical therapy procedures in common use by those engaged in treating the injuries of athletes are equally of value in treating the same type of injury wherever it occurs The procedures to be most effective must be instituted early, chosen intelligently, carrid out gently but intensively, and continued until the pathological process initiated by the trauma has been replaced by normal tissue activity.

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DIETOTHERAPY

By Sister Maude Behrman, BS and Miriam Adams, BS

Introduction—A review of literature for the year 1937 for new work in Dietotherapy finds most of the recent literature to be revolving around the vitamins Since most of the work is still in the experimental stage, no attempt has been made to include much of that literature in detail Rowe has published a new book this year which includes revised "elimination diets" superior to those previously advocated

Vitamin therapy is important in the treatment of arthritis. Every individual should be treated as an individual. If the patient is overweight, the diet is low calorie, high vitamin. If the patient is underweight, the diet used is of high caloric content as well as high vitamin. The banana is still the important carbohydrate food fed to patients with Celiac disease. The raw apple diet is discussed in the present volume.

Diets for diabetics no longer have the tendency to oscillate from one extreme to the other in the carbohydrate and fat content. A review in this volume follows Joslin's suggestion to avoid extremes Results of the work in nutrition done by the League of Nations have been showing up in improved health in other countries as well as in the United States

The effect of diet on tooth structure is still being carried on, with the belief that vitamin A and D play very important parts. This year the Harvard Dental School report that there may be a possible connection between vitamin C and pyorrhea.

The high vitamin A acid ash diet reviewed is considered, and recent articles have been reviewed and appear in this volume. A study of the diet of the (1136)

South African Negro shows why renal calculi is not present among them V Vermooten¹ reports that their diet is a simple, stable and uniform one, rich in vitamin A, and has acid ash and is extremely low in calcium

I. ADDISON'S DISEASE

The use of *low potassium diets* which are also *high in sodium chloride* content in Addison's disease have been reported by Sister Mary Victor in a paper which is included in the Proceedings of the Staff Meetings of the Mayo Clinic ²

Very good results in the treatment of this disease have been reported Large doses of sodium salts and injections of active extracts of the suprarenal cortex are given, along with the diet in which the restriction of potassium is the important feature. It has been found that these patients often have poor appetites Unless the patient is co-operative while on this diet, and the food is all eaten, the purpose of the diet is defeated To do this, it is suggested that the food should be served very attractively and should also be tasty Accurate check should also be kept on the amount of food served to the patient as well as an accurate account kept of the actual intake It is difficult to find accurate up to date tables of potassium values in foods Splendid charts are included in this report. The foods are grouped into classes containing similar amounts of potassium, thus making it much easier to calculate the potassium value of the diet The figures have been taken from other tables, and much is the result of actual analyses of foods which they have used, after they have been specially prepared.

A diet in which the potassium content does not exceed two grams is given. It is an adequate diet, providing 2700 calories and 70 grams of protein. If it is necessary to have a higher caloric value to the diet, cream, butter and mayonnaise are suggested as possible conveyors of more calories in concentrated form. The diet is deficient in vitamin B, therefore it would be wise to give a vitamin B concentrate. Brewer's yeast was suggested in the first paragraph of this review. Only white bread and refined cereals may be used, because the dark ones are too high in potassium.

The menu is shown below as a guide to anyone who might be interested in trying the diet

The first meal consists of

Fruit (chosen from group containing approximately 200 mg per 100 grams), average size serving

Cereal (only white cereals are used — no whole grains), average size serving

Egg. 1

Bacon, 2 small strips

Bread, white, I slice

Butter, 1 square

Cream, 1/2 cup, scant

(One cup of weak coffee and two cups of weak tea are used or allowed daily)

The second meal for the day includes the following

Meat, specially cooked as will be explained, 1 fairly large serving

Potato, specially cooked, 1 serving

Vegetable (chosen from the group containing approximately 75 mg per 100 grams), 1 serving

Bread, white, 1 slice Butter, 2 squares

Fruit (chosen from the group containing approximately 125 mg per 100 grams), 1 serving

Cream, 2 tablespoons

Milk, 1 glass

For the third meal we find the following:

Egg, 1.

Rice, 1 serving.

Vegetable (chosen from the group containing approximately 300 mg per 100 grams), 1 serving

Mayonnaise, 1 tablespoon

Bread, white, 1 slice

Butter, 2 squares

Fruit (chosen from the group containing approximately 125 mg per 100 grams), ½ cup.

Cream, 2 tablespoons

Cheese, 1 cubic inch

The following foods are listed as being high in potassium, and should therefore be avoided:

Soups and broths containing meat stock or meat extracts

Gravies

Catsup, chili sauce and mustard

Dried fruits such as dried apples, prunes, dates, figs, raisins

Nuts and peanut butter

Molasses

Caviar

Fruit juices except those listed

Chocolate and cocoa in the form of beverage or in the form of candy

Fruit drinks except those specially prepared Postum

Bran

Tartrate baking powders

Spinach except specially cooked

Numerous substitutes are given which should make the planning and serving of this diet more interesting and without question appeal to the patient with Addison's disease

Sister Victor makes it possible to include more food in the diet than would be possible under ordinary circumstances, by specially cooking foods, thereby decreasing the potassium content. She says, "vegetables like potatoes, turnips, and so forth should be peeled and cut into small pieces about \(^3\)4 inch (19 mm) square and \(^1\)8 inch (3 mm) thick. Cabbage, spinach and the other leafy vegetables should be shredded. Cauliflower

should be broken into flowerets, and the flowerets particularly quartered. Brussels sprouts should likewise be partially quartered String beans and asparagus should be cut into ½ inch (12 mm) pieces Peas are left whole For cooking use a deep, narrow kettle rather than one that is wide and shallow After being prepared, the vegetables should plunged into boiling salted water Use 11/2 teaspoons of salt for each quart of water Cook gently as too vigorous boiling may cause the vegetable to break into pieces" The proportion of water to the vegetable as well as the approximate length of cooking are given in the table for special cooking of vegetables This is usually one cup of vegetable to six to eight cups of water and the cooking usually from 10 to 15 minutes uncovered, except the root vegetables which are cooked covered for 25 to 40 minutes Beets, corn and tomatoes are cooked in parchment paper The cooking time may vary with the vegetables When they are tender the same procedure is followed as is used in cooking any vegetable The water is drained off and they are dried over the flame, and then served after they have been seasoned with salt and butter or cream

The directions for cooking meat are very simple. She says that as much as 75 per cent of the potassium content is reduced. The meat is cut up into small pieces and placed in a piece of parchment paper and then entirely immersed in water. If evaporation takes place the water must be replaced. It is better to cook in a covered vessel. After the meat has cooked this way for two hours, simmering not boiling in this salted water, it is removed. The meat is served with the juices surrounding it in the bag. It may be served scalloped, creamed, in sandwiches or salads, stews or in

omelettes The large amount of sodium chloride is sometimes difficult to give. The following recipe will take care of the sodium chloride and is not difficult to get the patient to take it

The following recipe makes one quart and may be used as a beverage during the day

Concentrated fruit beverage, 3 ounces or ½ cup

Sodium chloride, 10 grams or 2 teaspoons Sodium citrate, 5 grams or 1 teaspoon Water to make 1 quart

This should be served ice cold

Keys believes that more work will soon open up as more is learned about potassium and mineral metabolism. They have already found that potassium intake may be of importance in myasthenia gravis, neurasthenias and chronic nervous exhaustion.

II. ANEMIA

Dr G R Minot3 says that one of the symptoms of defective nutrition is often anemia It should be kept in mind that the symptoms must be eradicated or placed under control, and the patient taught to keep reserve supplies on hand in the body, if he is to remain in good nutritional state for the rest of his life If liver extract is needed there is a possibility that he will need it for the rest of his life or a relapse of his disease will occur If the causes of the anemia are corrected it may not be necessary to Each individual is a special take iron problem He suggests that liver extract "is at least 60 times as effective when injected as that taken by mouth"

There is no special diet for anemia Foods rich in blood building constituents should be emphasized. The following list of foods are arranged according to their potency as blood builders (Whipple)

- 1 Liver
- 2 Kidney
- 3 Gizzards
- 4 Skeletal muscles from beef or lamb, brains or pancreas
- 5 Fruits, such as apricots, peaches, prunes, raisins, either fresh, dried or canned
- 6 Leafy vegetables

A well balanced adequate diet is necessary Large amounts of liver need not be taken, because as Minot says, "the material potent for pernicious anemia can best be administered in extract form" The patient should be advised to eat some liver. It is a very good food because it contains protein of high biological value. The following points should be taken into consideration by a physician when he is giving advice to his patient about diet.

First — Should the patient gain or lose weight?

Second—What is the state of the digestive system?

Third—Can the patient tolerate fats?

Fourth—Is the patient hypersensitive to any foods?

Minot says that the diet is more important in the prevention of anemia than it is in the treatment

As soon as a patient passes from the state of good nutrition to that of partially deficient nutrition something should be done at once to correct it. He believes a dietary history carefully taken and evaluated is most helpful. Much suffering from anemia might be avoided by all persons, especially women, if an "optimal diet" were taken throughout life

III. ANOREXIA

F H von Hoffe⁴ states that in all that has been written about the treatment in anorexia, the value of a *special diet* in treating these cases has not been emphasized

Over a period of time these children suffering from anorexia demand and consume a high carbohydrate diet, and usually milk and carbohydrate are the chief standby Von Hoffe states that with this high carbohydrate diet in mind, and also with the knowledge that young children on the commonly prescribed diet for celiac disease usually have very keen appetites, it was thought logical to prescribe a diet low in carbohydrate and milk or milk free. The result of this diet in regaining the appetite was striking. If there was no response in two weeks, there was at once a suspicion that there was some error in the routine

The meals for these children suffering from anorexia were planned as follows

Breakfast

Bacon Egg

A small piece of Swedish rye bread

Butter

Stewed fruit

A well ripened banana

Orange juice or any other fruit juice may be included

DINNER

Broth or soup (no cream soup) Meat

Vegetables (no potatoes)

Gelatin or

Stewed fruit

A well ripened banana

SUPPER

Broth or soup (no cream soup) Vegetables or A fruit or vegetable salad

A Ifult of vegetable said

Cottage cheese

A small piece of Swedish rye bread

Butter

Gelatin or

Stewed fruit

A well ripened banana

These patients receive no milk, cereal, potato, puddings, and bread-stuffs other than a small quantity of Swedish rye bread. The fruits are stewed with little or no sugar

There must be proper management in the home. It is necessary that the mother and all the others leave the child while he is having his meal, unless he is too young to feed himself. At the end of 20 minutes things should be taken off the table regardless of how little has been consumed.

It is necessary that the "little patients" are not overtired "Most animals will refuse to eat when tired, and it is unnecessary to state here that no method of treating anorexia can be successful if we are dealing with a nervous or physically tired child"

In the course of a week the progress in an average case is evident. However, many children will take the diet for two weeks before a striking change in appetite takes place, and occasionally three weeks are required before a change takes place. When the patient becomes ravenously hungry, sparing amounts of carbohydrate are added and later small amounts of milk given. The child is kept on a relatively low carbohydrate and low milk diet for an indefinite time. In view of the fact that they are on a relatively low calcium diet, the children are given calcium.

The child does not infrequently lose weight, in fact it is not uncommon during the first week or two to lose a pound, but with the improvement of the appetite this loss is soon made up

IV. DIABETES

An excellent example of the inconsistency of nature concerning the percentage of sugar in foods is shown by E P Joslin ⁵ He believes that dietitians as well as physicians are apt to become too much fascinated by the calculation of diets and overlook such variations as he shows in the following example Two apples are shown, the one contained

63 per cent of carbohydrate, and the total carbohydrate for the apple was 16 grams or about four teaspoons The other apple contained 17 per cent of carbohydrate or 37 grams or nine teaspoons of sugar He hopes that one may see from this example how foolish it is to calculate diabetic diets using decimal points He says, "one must remember that one deals not with analyses of an individual portion of a special food, but in the best tables one is dealing with multiple and average estimations of food " He believes that the teaching of the diabetic diets should become more simple Concerning the content of the diet, he says that today most doctors agree that the carbohydrate of the diet should be between 100 and 200 grams The protein should be the same as that for a normal individual, that is, one gram of protein per kilogram of body weight. The fat content of the diet should be sufficient to make up the caloric needs. One should guard against overnutrition

He goes on to show how simple it is to work out a diet consisting of 150 grams of carbohydrate One slice of bread weighs approximately 30 grams or one ounce and contains approximately 18 grams of carbohydrate If a patient is told that he may eat three slices of bread and three oranges he would have 100 grams of carbohydrate taken care of The orange contains 15 in his diet grams of carbohydrate At the same time he may be given a list of equivalents for one slice of bread or one orange for variation in his menus. One-half of an average sized serving of cereal contains about ten grams of carbohydrate Then, Joslin goes on to say that experience has taught him that few diabetics can eat more than 20 grams of carbohydrate in five and ten per cent vegetables, even though they are allowed to eat all that they may want One-half pint of milk contains 12 grams and a quarter of a pint of cream contains four grams of carbohydrate. We now have 150 grams of carbohydrate for 24 hours to be divided as the doctor suggests. Putting it more plainly it appears as follows.

| Amount of | |
|--|---|
| Carbohydrat | e |
| ın grams | |
| 3 slices of bread (1 slice contains 18 | |
| grams of carbohydrate) 54 | |
| 3 oranges (one orange contains 15 | |
| grams of carbohydrate) 45 | |
| One-half of an average serving of | |
| cereal 10 | |
| Assortment of 5 per cent and 10 per | |
| cent vegetables 20 | |
| One-half pint of milk 12 | |
| One-quarter of a pint of cream 4 | |
| | |

145 grams

The meals of a diabetic who is taking protamine insulin should not be crowded into a few hours as they sometimes are in hospitals They should be spread far apart He suggests that small lunches be taken between meals The "peak load" of carbohydrate at meal time is thus lessened The steady and slow action of protamine is better cared for in this These lunches, of division of meals course, should be small and should be a part of the allowance for the day They are better taken in the middle of the morning, the middle of the afternoon, and upon retiring Insulin reaction from protamine insulin is far different from regular insulin There is more warning, and pure carbohydrate given as is given for regular insulin reaction is not so satisfactory Joslin suggests that proteins be used since the available glucose would be used more slowly and last over a longer period of time However, carbohydrates may also be given, but they should not be the concentrated ones The division of carbohydrate among the three meals should be done according to the needs of the patient

mark where the new insulin was first used, most of the carbohydrate is given at breakfast. Joslin believes in dividing it differently. He gives one-fifth of the total amount at breakfast, and two-fifths of the carbohydrate at dinner and supper.

H. H. Mason and G. E. Sly⁶ state that from time to time cases appear which have shown most of the symptoms and signs of diabetes mellitus, but do not respond to insulin. They report on one case that was resistant to insulin, but after substituting levulose and galactose for dextrose, the glycosuria almost disappeared. The diet was composed of milk, the lactose being absorbed as equal parts of dextrose and galactose, banana powder, of which a considerable part of the sugar is levulose, and meat, green vegetables and vitamins

V. DIARRHEA

After reading the article in the American Medical Journal by the Committee on Foods concerning the use of pectin in the treatment of diarrhea one is amazed to read the report by W C Alvarez 7 A small amount of agar or some other hygroscopic substance will produce in some individuals quite a large increase in the bulk of the stool These voluminous stools produced by taking agar often last only a short time, and are followed by a period of constipation The patient must shift from one régime to another Almstead and his every few weeks associates in the last few years have measured the amounts of cellulose, hemicellulose and lignin in foods and feces These three substances have been grouped together under one heading, "crude fiber" These substances differ in the way they go through the digestive tract, and also in their ability to increase the bulk of the stool The hemicellulose are most easily broken down by bacteria of the bowel. The end-products of this fermentation are identified as fatty acids In grazing animals they supply about one-quarter of the animals' needs

Williams and Almstead believe that cellulose is not a good substance for the relief of constipation. It holds little water and does not increase the bulk of the stool Agar is about 80 per cent hemicellulose, holds a great deal of water and is far more laxative because it increases the bulk of the stool Further work showed that the effectiveness of agar was not due to its water holding property, but due to the ability of agar to retain in the stool some of the lower volatile fatty acids which resulted from the bacterial digestion of the hemicellulose

Work needs to be done to investigate why some fruits are mildly laxative and others are not. Some work done by Alvarez made him think that the pectins might be responsible. Commercial solutions of pectins were decidedly laxative for some individuals, but for others it was not

The raw apple diet in the treatment of diarrhea in childhood is discussed in a report by the Council on Foods 8 Unfavorable reports have come in recently as well as numerous favorable reports It is believed that the pectin in the apple is the constituent which is of value in the treatment Pectin and agar have been used alone and have been found to be as good as raw apple pulp in the results Pectin has colloidal properties and it is believed that these properties help to remove the toxic substances causing the diarrhea Its buffering action as well as the galacturonic acid content may also serve its purpose

Comparing apple powder with apple pulp, the powder has been found to be superior for children under one year of age. It is recommended that the powder

be given in "from four to ten per cent solutions in amounts varying from a total of 24 to 36 grams for babies under one year or from 80 to 100 grams for older children". The powder may be dissolved in skimmed milk or boiled water.

For mild cases found in young infants Leffkowitz suggests that a mixture be made consisting of equal parts of skimmed milk and water with five per cent apple powder dissolved in it. The mixture is given in the volume which the infant is accustomed to taking. No sugar is given during the first two or three days.

Normal feedings are gradually resumed At the end of the third day a five per cent dextrin maltose preparation is given. After four or five days the apple powder is decreased and milk and sugar increased. This apple powder has been found to be very suitable in the treatment of diarrhea, but fluid intake must be guarded, and the transition from one diet to another must be done under the direct supervision of a competent pediatric doctor.

VI ECZEMA

H Finkelstein⁹ believes that diet in the treatment of eczema in infants and children plays an important part states that for years it has been known that the addition of from 10 to 15 grams of protein powder such as calcium caseinate not only facilitates normal development but almost always leads to a cure of the dermatosis within three to four Therefore it is concluded that weeks mother's milk is not an entirely adequate diet for children with eczema Some necessary substance essential for normal composition of the skin and normal metabolism of the epidermis must either be absent from breast milk or present in insufficient amounts, and this substance must be contained in the protein of the diet "In other words, seborrheic eczema in young babies is due to a specific insufficiency of food related to a low supply of protein"

With a minority of breast-fed infants the addition of protein has little or no effect but when a mixed feeding with cow's milk is prescribed there is a speedy recovery, the best results are obtained by using skimmed milk or buttermilk, that is a substance not only rich in protein but low in fat Therefore it is concluded that breast milk is unsuitable for children suffering from seborrheic eczema not only because there is something lacking in it which is contained in the protein but also because there is too much fat contained in it. Proof that the fat metabolism of the skin is involved, is found in the fact that seborrheic changes occur mainly in regions where there are numerous sebaceous glands, e g, the scalp, the margins of the eyelids and the genitalia Seborrheic eczema occurs regularly where there is a lack of vitamin B_2 in the diet Gyorgy spoke of a cutaneous factor in protein, breast milk contains little of it, cow's milk more and a considerable amount is found in liver, yeast, potatoes and kidney

The giving of an adequate amount of the cutaneous factor and the avoidance of too much fat are not the only prerequisites for recovery. There are several other conditions that must be fulfilled

First, there must be no dyspeptic disorder and no other infection. Seborrheic eczema never heals as long as diarrhea or a febrile complication is present. A large part of the cutaneous factor present in food is destroyed or lost in the thin stool when there is diarrhea. There is also a greater need for all vitamins during infection.

Second, seborrheic eczema never heals if the child does not gain weight even though infection and diarrhea are not present. Curing dystrophy is not difficult, usually it can be done by giving the baby plenty of calories and a large amount of carbohydrate. A dystrophic child requires one and one-half to two times as many calories as a normal child of the same weight. The dystrophic child needs a large amount of carbohydrate, which is best given in the form of malt extract and flour.

Third, seborrheic eczema never heals as long as there is a pyogenic infection of the eruptions. Dietary treatment is often, but not always, sufficient to overcome the cutaneous complication.

The dietetic treatment of true eczema, Finkelstein states, is entirely different from that of seborreic eczema. A diet which will cure the latter will be of no value and may even be harmful

The treatment of true eczema has to be dietetic, for constitutional eczema is beyond doubt alimentary in origin "The disorder is surely related to the milk This can always be demonstrated Eczema in a baby who drinks a quart of milk per day will improve in a few days if the milk is reduced to a few ounces, and on the other hand, an increased amount of milk will make the condition worse. The same holds true, though to a lesser degree, if sodium chloride is added to the vegetables"

It must be remembered that the sensitivity to inflammatory irritations as well as the intensity of the inflammatory reaction depends to some degree on the water and sodium chloride content of the tissue. In the first years of life the tendency to increased retention of water and salt is normally more marked than it is later, in children with lymphophilia of the skin the tendency may reach a pathologic stage. For lymphophilic chil-

dren even the amount of salt contained in milk is too great, especially if a large amount of carbohydrate is given at the same time, for the carbohydrate favors the retention of water and salt

If considerable exudation is present, a diet containing a small amount of milk and carbohydrate is indicated—200 to 300 cc of milk per day with fruits and vegetables and small amounts of cereal In order to increase the protein content, from 10 to 20 grams of cottage cheese, meat or calcium caseinate can be added. The eczema sometimes is only changed from moist to dry and is not cured "That is the angioneurotic-prurigenous component of eczema is not affected by the treatment"

In fighting this angioneurotic-prurigenous component it is useless to replace milk with other animal proteins. Therefore a diet entirely of vegetables has been tried. Soy bean milk has been recommended by Hill and others. Finkelstein states that soy bean milk is better than cow's milk and the condition is often improved or cured, but the improvement is slow.

Ouicker and surer results are obtained by a diet consisting mainly of fruit, vegetables and free from fat For the first two days only fruit and rice are given, then cereals, breads, vegetables, salad, tomatoes, and potatoes are added 15 given Also from 10 to 20 grams of vegetable protein is given However, this restricted diet can not be used for a long period of time because of the lack of sufficient protein. After marked signs of improvement are shown certain additions are made, first, buttermilk or cottage cheese is added, then later meat, and later vegetable fat Only one food is added at a time and in small quantities

It seems that tolerance is improved with this basic diet lacking fat and animal protein. Slowly other foods can be

added which previously had been visibly harmful Gradually an adequate diet suited to the individual is attained and the skin remains clear. From time to time it is well for a period of time to strictly control the diet. Fortunately, eczema in the majority of cases has a tendency to improve spontaneously and finally to disappear after the third year, so that a more liberal diet can be used.

VII. FOODS

1. Beer

These facts were obtained from a publication of the United Brewers Industrial Foundation (21 East 40th Street, New York, N Y)

Dr Winfield S Hubbard, formally with the United States Food and Drug Administration, says, "Beer is a food

easily assimilated as beer——it is almost ready to be absorbed through the intestinal wall as soon as it leaves the mouth"

The analysis of 385 samples of American lager beer with alcohol content of 365 per cent by weight and extract 513 per cent shows that the nutritive value of one pint of beer is 215 calories. An eight ounce glass contains 108 calories, and the average beer bottle or can, holding 12 ounces has 163 calories.

The equivalent of the caloric value of one pint of beer is approximately one of the following

- 1 ounce butter
- 111/1 ounces potatoes
- 10 fluidounces milk
- 31/4 ounces bread
- 16 ounces apples
- 111/2 ounces lean fish meat
 - 4 ounces medium fatty beef
- 5 ounces lean beef
- 3 average eggs

Scientists have agreed that beer has a definite tonic value. Beer is a healthful, nourishing food beverage because the resins of the hops have tonic effect.

2. Gelatin

The Council on Foods¹⁰ states that in the last few years much attention has heen directed toward the amino acid makeup of gelatin. Publicity given out by biased or unscientifically trained persons has been favorable and unfavorable. and in the opinion of the Council often misleading It has been believed that because gelatin is classed as an incomplete protein, biochemically it should be avoided, and just as enthusiastically it has been recommended as a means of increasing the protein of the diet Since the discovery of the great success reported in the use of amino-acetic acid for patients with certain myopathies, firms have advertised the use of gelatin in the treatment of muscular dystrophies The Council in this report has endeavored to evaluate the nutritional claims for gelatin from the available evidence

"Gelatin is a protein derived from collagen present in the white fibrous tissues" The pure protein composition of dried gelatin is usually from 85 to 90 per cent. For typical analysis of gelatin and gelatin dessert powder one is referred to the Table 1 which appeared in this report.

Gelatin is readily digested by the proteolytic enzymes of the alimentary tract but it is not partially digested to begin with, but from the practical point of view its ready digestibility does not give it superiority over the common proteins

The analysis of the amino acids by Dakin in 1920 with the additional data obtained by later investigators is found in Table 2.

TABLE 1—TYPICAL ANALYSIS OF GELATIN AND GELATIN DESSERT POWDER

| | Gelatın Per cent | Gelatin Dessert Powder Per cent |
|---|---|--|
| Moisture Ash Fat (ether extract) Protein (N x 5 5) Carbohydrates Tartaric or citric acid Added flavor Added color Calories per gram (approximate) | 10 0 1 2 0 0 88 5 0 0 none none none | 0 8 0 2 0 0 11 0 86 0 2 0 present present |
| | | |

TABLE 2-AMINO ACIDS IN GELATIN

| | Dakın | Other Investigators |
|---|---|---|
| Aminoacetic acid Alanine Valine Leucine Isoleucine Serine Phenylalanine Tryosine Proline Hydroxyproline Aspartic acid Glutamic acid | 25 5 8 7 0 0 7 1 0 0 0 4 1 4 0 01 9 5 14 1 3 4 5 8 | 25 7 (Bergmann) 0 0 (Looney, Hanle) 19 7 (Bergmann) 14 4 (Bergmann) |
| Hydroxyglutam c acid Histidine Arginine Lysine Cystine Methionine Tryptophane | 00098259 | 0 16 (Jones, Gersdorff & Moeller) (Looney, Folin & Looney) 0 97 (Baernstein) 0 0 (May & Rose) (Looney, Folin & Looney) (Jones, Gersdorff & Moeller) |

By means of the available data, gelatin may be classed as an incomplete protein because it lacks or contains too low a concentration of isoleucine, tryptophane and methionine

In the opinion of the Council the amino acid composition of gelatin is of no practical disadvantage unless gelatin is the sole source of protein in the diet

An ordinary serving of gelatin dessert contains about 25 grams of gelatin A concentration of gelatin as high as ten per cent can be made into a hot soup However it requires considerable ingenuity to formulate a menu that contains more than about one ounce of dry gelatin per day

The use of gelatin (containing 25 per cent of aminoacetic acid) in the treatment of the myopathies has been mentioned. From 20 to 30 grams of aminoacetic acid is usually the dosage in the treatment of myasthenia gravis or pseudohypertrophic muscular dystrophy. Therefore gelatin can give only a small portion of this dosage.

In the opinion of the Council, the claim that gelatin is an aid in the digestion of milk is not established. The present evidence shows that gelatin has no special significance as a source of amino acids in the diet.

VIII. NUTRITION

1. Nutrition

E N Todhunter¹¹ discusses the possibility of some foods taken into the body, but because of improper balance they are not utilized. Calcium of some foods may be rendered useless by the presence of foods containing oxalic acid combination of oxalic acid and calcium forms an insoluble calcium oxalate Rowntree has shown that vitamin A absorption is interfered with in the presence of mineral oil Investigators have shown that mineral oil renders carotene or vitamin A unavailable to the body, since the mineral oil shows a preferential solubility for the vitamin and prevents its intestinal absorption. A high intake of calcium and low phosphorus may result in rickets, especially if the vitamin D is deficient

An example of the importance of an optimum diet is given A group of growing boys were given in addition to an adequate diet one pint of milk extra every day. Over a period of four years, the average weight gain and height of the boys receiving the improved diet was almost double that of the boys who continued on their original diet.

2. Nutrition and Old Age

Under Current Comment¹² an article appears which seems to the Reviewer worth while mentioning since much stress is being put on the importance of diet and old age at the present time This has been especially stressed since the Rockefeller Foundation has "received a grant of \$42,000 to the Laboratory of Animal Nutrition at Cornell University for the study of nutrition problems of maturity and old age " The author mentions the "negative correlation between growth rate and longevity as brought out by C M McCay and M F Crowell 13 Lord Francis Bacon is quoted as follows (1561-1626)

- 1 The cure of diseases requires temporary medicines but longevity is to be procured by diet
- 2 It seems to be approved that a spare and almost Pythagorean diet produces longevity
- 3 Animals which come later to perfection (I am not speaking of growth in stature but only of the other steps to maturity as man puts out first his teeth, then his signs of puberty, then his beard, etc.) are longer lived, for it indicates that the periods return in wider circles
- 4 To grow long and slowly is a sign of longevity and the taller the stature the better the sign. But on the other hand, rapid growth to greater stature is a bad sign, but to a shorter stature less bad

- 5 I would have men duly to observe and distinguish that the same things that conduce health do not always conduce to longevity
- 6 Again there are other things very beneficial in prolonging life yet they are not without danger to the health unless guarded against by proper means

Cornell investigators have covered a period of investigating of four years with rats that were divided into groups which were as nearly homogeneous as possible. They found that the animals which grew more slowly to maturity because of limited calories but for whom an otherwise adequate diet was allowed, appeared physiologically young for longer periods of time and at the same time lived longer. It was also found that females lived longer than the males. The question still remains, however, "Can the ageing process be controlled by diet?"

3. Nutrition and Good Teeth

J O McCall¹⁴ says that the term good health as used by the dentist means that the teeth are of "good enamel structure, resistant to decay, and surrounded by healthy gums" He says that children who have poor teeth never "exhibit that glowing condition known as perfect health"

The great number of preschool children who have defective teeth today prove that it is not neglect of the tooth brush or failure to masticate coarse food as many would have us believe

The crowns of the deciduous teeth are fully formed during fetal life. This stresses the importance of the proper dietary habits of the mother. It cannot always be said, that it is true, if a baby has good skeletal development, he will also have good teeth. He goes on, as many others searching for the substance responsible for these good teeth. Since

the foundation structure of teeth is phosphorus and calcium, it should be the most reasonable thing to include in abundance or in proper amounts to prevent decay. A three-year-old child requires a little over one gram of calcium daily. The pregnant mother requires one and one-fourth grams daily. Vegetables alone cannot supply this amount. Milk is absolutely necessary.

The phosphorus requirement for the three-year-old child is one and one-fourth grams, and for the pregnant mother it should be one and one-half grams. Phosphorus is found in milk, eggs, whole grain cereals, as well as vegetables. Since McCall believes that the diet should be alkaline forming, he discourages the use of the egg and the cereal in large amounts and encourages the use of milk, fruits and vegetables, which will produce an alkaline ash

Vitamins A, D, C are the most important vitamins to include in the diet for tooth structure. Since vitamin D is poorly represented in the average dietary, the importance of taking cod-liver oil or irradiated milk follows. An alkaline ash diet is made possible by using an abundance of green leafy vegetables, and the use of potato to supply part of the carbohydrate usually supplied by cereals or cereal products. Fruits and milk also have an alkaline ash

On page 1148 are two sample menus given in the JOURNAL which supply all the body needs as far as the proteins, fats and carbohydrates, minerals and vitamins are concerned. The alkaline excess is 67 53 cc.

The intake of sugar should be guarded because it favors the growth of lacto-bacillus acidophilus which is the predominating organism in dental decay

The refining process robs cereals and sugars of their minerals, therefore he suggests that one use molasses, brown

SAMPLE DAILY MENU FOR CHILD OF THREE YEARS

| | 7 | |
|----------|---------------------|-------------------|
| Time | Food | Portion |
| A.M. 645 | Water | 3∕4 cup |
| | Lemon juice | 1 tsp |
| 7 00 | Cod liver oil | 2 tsp |
| | Orange juice | 34 cup |
| | Cereal (oatmeal) | ⅓ cup |
| İ | Butter | $\frac{1}{2}$ tsp |
| | Sugar | 1 tsp |
| | Milk for cereal | $\frac{1}{2}$ cup |
| | Milk to drink | ½ cup |
| 10 00 | Tomato juice | 3∕4 cup |
| 11 15 | Water | $\frac{1}{2}$ cup |
| 11 30 | Baked potato (with | |
| i | jacket) | 1 medium |
| | Butter | $\frac{1}{2}$ tsp |
| | Beet tops | ⅓ cup |
| | Banana | 1 medium |
| | Mılk | 1 cup |
| F.M 300 | Mılk | 1 cup |
| 4 30 | Water | ½ cup |
| 5 45 | Broth | 34 cup |
| | Egg | 1 large |
| | Butter | $\frac{1}{2}$ tsp |
| | Carrots (whole raw) | 4 inch |
| | Dates | 4 |
| | Tomato juice | 3∕4 cup |
| | 1 | 1 |

From "Do You Want Your Baby To Have Good Teeth?" The Murry and Leonie Guggenheim Dental Clinic, New York City

sugar, sugar cane juice, maple sugar or honev

Prevention of tooth decay should begin during pregnancy A picture of a child with very poor teeth is shown The diet of the mother during pregnancy was chiefly meat, bread, no milk, took no cod-liver oil and ate very few vegetables and not much potato own health seemed good. An indication of vitamin C shortage in the child, he says, may show up in sore gums This is noted when the child rejects hard objects Orange juice or tomato juice should then be increased If the gums are very sore and these fruit juices or tomato juice burn the gums and irritate, then vitamin C concentrate tablets should be given

SAMPLE MENU FOR CHILD OF FIFTEEN YEARS

| Time | Food | Portion |
|-------------------|--|--|
| A.M. 7 30 7 45 | Water Cod liver oil Cereal (whole seed) Molasses Milk (Grade B)* Bread (whole wheat) Butter | 1 glass 2 tsp 1 cup 4 tsp 1 glass 2 slices 1 tsp |
| 10 00 12 00 | Water Carrots (raw)** Substituted by Beet 2x weekly Apple 2x weekly Potato Beet top (raw or cooked 5 minutes in covered pot with no water added after wash- ing) green cab- bage may be sub- | 1 glass 2 1 1 1 medium |
| | stituted Butter Banana† Water | 34 cup 2 tsp 1 1 glass |
| PM 300 | Milk Cookies Apricots (dried) | 1 glass 2 3 |
| 6 00 | Bean or split pea soup (heavy) Turnip Whole wheat bread (24 hours old) Substituted by Fish (once a week) Lean soup meat (spleen, heart, | 1½ cup ½ cup 4 slices 4 oz |
| | lung) once a week)‡ Egg (Grade B) (twice a week) Butter Fruit in season Milk | 3 oz 1 2 tsp 1 large 1 glass |
| 8 00 | Water | 1 glass |

Prepared by Frances Krasnow, Ph D, Head of the Department of Biochemistry, The Murry and Leonie Guggenheim Dental Clinic

Note Candy, ice cream, rolls, fresh bread, cake must be excluded from the diet. Total cost of diet is approximately 27-30 cents per day. The schedule may be applied to other school ages with proper adjustment of calories, and so forth

- * Extra milk desirable if income permits
- ** Fruit or fruit juice desirable if income permits
 - † Followed by milk if income permits
 - ‡ Beef and liver desirable if income permits

IX. PEPTIC ULCER

A. B Rivers¹⁵ says that there is a great difference of opinion regarding the selection of the proper diet for patients suffering from peptic ulcer

The diet used in the peptic ulcer should be non-irritating, adequate and should not cause a great secretion of acid. The diet should be such that neutralization of acids by combination is

permissible and that there is a choice of allowed foods

The following table gives the treatment of peptic ulcer by diet or alkalinization.

In the course of an exacerbation of an ulcer the patient is usually placed on frequent milk feedings as indicated in Diet A. Usually after restriction of their food intake to milk for several days the

DIET A

DIET B

| | Mılk cc | Cream cc | Milk cc | Cream cc | |
|------------------|----------------|-------------|----------------|-------------|--|
| A M 7 00 7 30 | 60 Powder 1 | 60 | 45 Powder 1 | 45 | Orange juice 2 tbsp dilut Cereal |
| 8 00 8 30 | 60 | 60 | Breakfast | | Cream |
| 9 00 9 30 | 60 Powder 2 | 60 | 45 Powder 2 | 45 | 1/2 sq butte |
| 10 00 10.30 | 60 Powder 1 | 60 | 45 | 45 | |
| 11 00 11 30 | 60 Powder 2 | 60 | 45 Powder 1 | 45 | (Cream soup egg |
| 12 00 12 30 | 60 Powder 1 | 60 | Dinner | | Toast 1/2 sq. butte Bland desse |
| P M 1 00 1 30 | 60 Powder 2 | 60 | 45 Powder 2 | 45 | (|
| 2 00 2 30 | 60 | 60 | 45 | 45 | |
| 3 00 3 30 | 60 Powder 1 | 60 | 45 Powder 1 | 45 | |
| 4 00 4 30 | 60 Powder 2 | 60 | 45 | 45 | (Cereal |
| 5 00 5 30 | 60 Powder 1 | 60 | 45 Powder 2 | 45 | Rice Baked pota |
| 6 00 6 30 | 60 Powder 2 | 60 | Supper | | Toast |
| 7 00 7 30 | 60 Powder 1 | 60 | 45 Powder 1 | 45 | Bland dess |
| 8 00 8 30 | 60 Powder 2 | 60 | 45 Powder 2 | 45 | |
| 9 00 | 60 | 60 | 45 | 45 | |

Cereals allowed Farina, cream of wheat, rice, strained oatmeal, Meads, baby Ralston

Eggs may be prepared soft cooked, coddled, shirred, poached

Cream soup may be made of vegetables as listed and must be strained through a fine strainer

Desserts custards, plain jello, simple puddings such as rice, tapioca, cornstarch, blanc mange, ice cream, bavarian cream

 $0.5~\mathrm{gm}$ calcium carbonate and $0.3~\mathrm{gm}$ sodium bicarbonate $15~\mathrm{gm}$ calcium carbonate and $0.4~\mathrm{gm}$ magnesium oxide

DIET C

DIET D

| | | ,, | | |
|--|--|---|--|--|
| | Milk and Alkalis as in Diet B | Mılk cc | Cream cc | |
| A M 7 00 7 30 8 00 9 30 9 30 10 00 10 30 11 00 12 3 P.M 1 0 1 3 2 0 2 3 3 0 3 3 3 4 0 4 3 5 0 6 3 7 0 7 3 6 | Breakfast Orange juice Cereal Cream Egg Toast, butter Dinner Cream soup Meat Mashed potatoes Pureed vegetable Toast, butter Custard Milk Supper Baked potato Cottage cheese Pureed vegetable Cottage cheese Pureed vegetable | Powder 1 Breakfast Powder 2 120 Powder 1 Dinner Powder 2 120 Powder 1 Supper Powder 2 | 60 | Cooked cereal Cream Soft cooked egg Toast, butter Sugar Stewed fruit Orange juice Postum Cream soup Meat Mashed potatoes Pureed vegetables Toast, butter Custard Milk Baked potato Cottage cheese Pureed vegetable Toast, butter Stewed fruit Cream Milk |
| 8 (8 3 9 (| Stewed fruit | Powder 1 120 | 60 | |
| | Cereals to be allowed in addition to those in addition to those in Diet B Maltomeal, corrumeal Eggs in addition to Diet B may be scrambled in double boiler, souffle Desserts in addition to Diet B fruit allowed peaches, pears, aprico (skinned and cooked untitender), applesauce machine in the service in t | n Diet C con- rice flakes Vegetab et stringbean a spinach, y previously o Meats d beef balls, oyster stev tal baked) After th tenderloin steamed, Dessert | rnflakes, poles allowed, calves live w, (meats of tender), baked, cres white | n addition to those in buffed rice, rice krispies, ed asparagus, young, squash, peas, youngs, cauliflower (if it has ith the individual) chicken, fish, scraped or, sweetbreads, strained can be broiled, steamed, add tender lamb chops, lean roast beef, boiled, amed potato cherries, ripe banana, range cake, plain hard |

pain disappears. Thereafter, the diet is increased to include foods given under Diet B. If there is no distress on the part of the patient from the food included in Diet B, the food intake is rapidly increased to include all substances in Diet C. After being hospitalized for about a week the patient is

given a rather liberal diet, as indicated in Diet D On leaving the hospital, states River, the patient is instructed as to Diet D and advised to stay on it for a month or six weeks. After this period a greater variety of meats as broiled beef, lamb chops, liver, chicken, lean roast beef are permissible. However, the

patient must restrict himself to vegetables which do not include much roughage

Patients who have a remission of ulcer usually start on Diet C. After a few days they are advanced to Diet D and kept on this diet during the rest of the time in the hospital "It is important that the food given to these patients be well prepared. There should be proper variations of menus and food should be served in a way to stimulate the patients' appetite"

X. RHEUMATISM

Dr Dorothy C. Hare¹⁶ states in her presidential address to the Section of Therapeutics of the Royal Society of Medicine, London, that they treated 12 cases of chronic rheumatics by diet alone so as to get an accurate result rheumatics were composed of the main types of muscular rheumatism, osteoarthritis and rheumatoid arthritis The patients were admitted to the Royal Free Hospital (the London School of Medicine for Women) The first week of admission they were put on a regular If possible the patients were up and around for several hours daily doing voluntary exercise in the physical therapy department The routine for the diet was in two parts The first lasted two weeks, and the food eaten was entirely uncooked The diet averaged 2000 calories daily and consisted of the following.

Vegetables, 14 ounces (salads, tomatoes, roots)

Citrus fruit, 8 ounces (oranges, lemons, grapefruit)

Apple, 6 ounces

Dried fruit, 4 ounces (apricots, prunes, raisins)

Nuts, 2 ounces

Crushed oats, 3/4 ounces (served after soaking)

Sugar, 1 lump

Salad oil or mayonnaise, 2 ounces

Cream, 20 per cent, 3 ounces M₁lk, 12 ounces No salt. Fluids, tea and water, unrestricted

This diet yielded approximately carbohydrate 145 grams, protein 35 grams and fat 143 grams

After two weeks the following daily addition of cooked foods were made

Vegetable soup
Egg . . 1
Meat . . 2 ounces
Bread . . . 2 ounces

and as uncooked additions.

 $\begin{array}{ccc} \text{Butter} & . & 1 \text{ ounce} \\ \text{Cheese} & 1 \text{ ounce} \\ \text{Milk} & 20 \text{ ounces} \end{array}$

No salt was added except that present ordinarily in the food. The oil and cream was reduced as necessary. This diet then contained approximately carbohydrate 146 grams, protein 66 grams, fat 142 grams equal to 2200 calories. The patient was given this last diet for a period of weeks or months.

Eight of the 12 patients felt definitely better within one to four weeks. Of the remaining four, two improved until five or six weeks were reached and then had a relapse, and the other two found no relief at all. The improvement of these cases consisted of decreased pain, stiffness and swelling "Pain arising in joints with active disease of bone and toxic symptoms were not relieved. The cases of muscular rheumatism uncomplicated by definite arthritis gave the best response."

Patients suffering with rheumatoid arthritis gained some relief from pain and stiffness at first but for many weeks the toxic symptoms remained apparently uninfluenced. Only one patient remained on the continuous diet treatment for several months and she made a remarkable improvement.

Dr Hare attributes the rapid recovery to the low sodium content of the diet. The amount of sodium in the vegetable foods was very small and no added salt was allowed in the diet, therefore there was a rapid loss of tissue fluid. Undernutrition was not a factor in producing the results. Dr. Hare insisted on the addition of adequate protein and fat to the vegetable diet, and states that the large supply of Vitamins B and C was of great value.

XI SCHIZOPHRENIA

G W B James, Rudolf Freudenberg, and A Taudy Cannon¹⁷ state that in phase 2 of the insulin shock treatment of Schizophrenia, this being three to four hours after the insulin is given, a nasal tube is passed. Then, seven ounces of sugar is given in 500 cc of tea Also at the same time seven ounces of sugar with milk, cream and three eggs are given to patients refusing to eat their meals After the nasal tube is removed waking should take place 20 to 30 min-The patient is then given utes later cake or biscuits and milk to drink. The patient rests in bed about one-half hour and then an ordinary lunch is served It is important that sufficient food is taken at all subsequent meals, or there may be late hypoglycemic symptoms All the food consumed during the rest of the day should be recorded

XII. URINARY CALCULUS

Work continues to be done as further investigation goes on to discover the importance of vitamin A as a dietary factor in the management of Urinary Calculus W M Kearns¹⁸ says: "Unquestionably the most important factor in the production of urinary stones is diet, and particularly the part played by

vitamin A deficiency " Asborne, Mendell, Von Leersum and McCollum have all concluded that vitamin A plays a very important part McCarrison has found that excess lime in the diet which is otherwise deficient in proteins, fat soluble vitamins and vitamin C, favors the formation of stones This conforms with the idea that long continued use of hard water may tend toward stone formation Vitamin A in the diet tends toward the prevention of stones even in the presence of excess intake of lime It is worthy of note that there has been a decline in the incidence of stone in children in countries where there has been widespread practice of including vitamin A In the less in the diet of children civilized countries this decline has not been noted

Higgins has made use of the vitamin A feeding and the use of acid ash diets for calculous patients There is not much danger of a vitamin A deficiency in the average diet, but often because of poverty, "capricious appetite" which may be the result of poor dietary habits, gastrointestinal disease, liver disturbances, or poor utilization of vitamin A, the diet may not supply sufficient vitamin A At present there is a test which may prove to be of much value later on. which determines whether there is a vitamin A deficiency and predicts the response to therapy It has been found that urmary infections are the result of epithelial changes due to vitamin A deficiency Before the diet therapy is started, two halibut liver oil capsules are given three times a day If this is not well tolerated or if there is faulty absorption, the intramuscular injections of concentrated vitamin A liver oil are resorted to preparation for injection is the oil from the liver of the black sea bass which contains ten times the potency of halibut liver oil Brewer's yeast tablets are given three times daily Vitamin A rich foods are given in abundance patient is excreting calcium oxalate crystals, tomatoes and rhubarb are omitted from the diet One must guard against omitting foods from the diet which are rich in vitamin A If, for instance, the patient is excreting uratic crystals, such food as liver, sweetbreads, and kidney should be restricted because of their purine content On the other hand, liver is one of the best sources of vitamin A and the cause of precipitation due to lack of vitamin A should be treated first Most stones occur in alkaline urine, therefore the acid ash diet is the most commonly used

Kearns reports recently that large renal calculus have been dissolved. When this takes place he finds that there is an unusual excretion of lactic acid in the urine of the patient. Properties of the acid show that it has strong affinity for calcium with which it unites to form the soluble calcium lactate. Lactic acid occurs abundantly in foods, such as buttermilk, beer, sour wine, and sauerkraut juice. These foods should be given to these patients to insure the presence of lactic acid in the urine. B acidophilus milk is also suggested, as well as doses of lactic acid by mouth if tolerated

XIII VITAMINS

Now that it has been made possible to isolate the vitamins and to determine the amount necessary for individuals, it is worthwhile to note the possibilities of filling the vitamin quota. The United States Government has published a bulletin recently from which it is possible to calculate the amount of vitamins in various foods. One serving of spinach will give the daily requirement of vitamin A, or one serving of carrots daily, or one pint of milk plus four tablespoons of

butter The vitamin B requirement is surprisingly difficult to fill One serving of a whole grain cereal, plus whole grain bread three or four times during the day, plus one pint of milk, plus one egg and two servings of vegetables and one serving of orange juice will give the daily minimum quota One-half cup of most any citric fruit juice will fill our vitamin C quota for the day Tomato juice may be substituted

It is also very interesting to note that cooking in ordinary ways does not destroy the properties of the vitamins, except vitamin G Daniell, Kennedy and Munsell¹⁹ report that orange juice refrigerated loses ten per cent of its vitamin C content Tomato juice loses three per cent in one hour in the refrigerator Three to four days causes a loss of 40 per cent Acid foods such as tomatoes and pineapple hold up well under the canning processes and no vitamin C is destroyed Bogert says that cooking for a long time in open kettles, copper cooking utensils and the addition of an alkalı lıke soda all favor the oxidation and destruction of the vitamins The importance of vitamin A in the diet has been shown by many investigators It has now been definitely established that it is an anti-infective vitamin epithelial structures are effected by lack or withdrawal of the vitamin A as is found in some gastro-intestinal diseases and diseases of the liver where vitamin Λ fat foods are restricted. With a break down of the tissue comes the invasion of bacteria Lesions of all sorts may be caused by the keratimization of the cells It is thought that this may be the cause of gastric ulcer, diarrhea, respiratory infections, etc 20 During hyperthyroidism, Abelin and Wendt have noted an increase in the vitamin \ requirement, in fact, all diseases where the metabolic rate is increased, increases the demand for vitamin A

The infant has also been found to come into the world with no vitamin A The colostrum provided the reserve infant in mother's milk is richer in vitamin A than the milk which is supplied later, which proves that nature does attempt to take care of the young In another review in this section the importance of vitamin A in the prevention of kidney stones has been mentioned V Vermooten²¹ reports that the diet of the South African Negro is a simple, stable and uniform diet, rich in the vitamin A, and has an acid ash as well as being extremely low in calcium South African Negro, he goes on to say, does not form renal calculi Mendel is thoroughly convinced that vitamin A plays an important part in the prevention of kidney stone and so does Kearns, as is shown in the review of his article in this section. Of course there are some who have reported no success in their attempts Sherman believes that vitamin A plays a very important part in longevity

Important work has been done with vitamin B therapy for alcohol addicts N Jolliffe, C. N. Colbert and P. M. Toffe?? say that a large part of the caloric intake of the alcoholic addict is derived from alcohol. Naturally he does not obtain sufficient vitamins and as a result we find alcoholic neuritis. The use of high vitamen B diet has proved most helpful in a case noted by the RIVIIWER The use of high vitamin B diets for prospective mothers is very important She should take enough for her own needs as well as that of the child One of the first signs of lack of vitamin B 15 anorexia There is a quantitative relationship between the number of days during which the appetite may be restored by giving vitamin B, the body

weight of the animal and the amount of vitamin given

Barnett Sure reported at an American Biochemical Society meeting that 1000 units of vitamin B_1 per day has proved very beneficial in the treatment of cardiac cases. Vitamin B consists of two fractions, the heat labile fraction of which the above material is concerned, and B_2 the heat stable group

It is now believed that there are at least six different vitamins in the heat stable group. There is only a certainty of three at the present. The first is the lacto flavin fraction already isolated in pure form. The second is vitamin B₆ the absence of which in the diet of the rat is responsible for characteristic deimatitis affecting the nose, eyes, ears, and is called rat pellagra. The third is the pellagra preventive factor which also prevents and cuies black tongue in dogs.

P L Day, W J Darby and W C Langston²³ show that riboflavin or lactoflavin is a significant factor in the prevention of catalact. Chase²⁴ says that regeneration of visual purple also requires the presence of a flavin.

Concerning vitamin C we learn that deficiencies of Cleads to the damage of blood vessel walls and degeneration of bone and other connective tissue Tiny hemorrhages in the skin or membranes is a result of vitamin C deficiency Because vicamin (is a water soluble vitamin, much is readily eliminated through the kidneys, depending upon the ability of the body to retain a certain degree Repair following the inclusion of vitaniin C in the diet is quite dramatic Wohlbach reports that "newly formed dentin, collagen, and bone matrix" can be seen after 24 hours Minor symptoms from lack of vitamin C may be fleeting pains in the legs and joints, bleeding gums and soreness and stiffness of joints

W H Eddy²⁵ says that the problem of vitamin D is still a live issue. He mentions the work of Windau in the Merck Jahresberichte in which three forms of vitamin D are described and that the one in tuna fish is mainly D₃ He mentions Drake's report in which it is maintained that there is no essential difference in the antirachitic property of vitamin D in cod-liver oil, mixed fish oils with high potency, irradiated cholesterol or irradiated milk. Heyman has reported that bile in the digestive tract is necessary for the proper absorption of vitamin D In the report of Eddy on the vitamins he does not feel that there is anything of importance to report on vitamin E Other vitamins have been mentioned but so little has been done that they do not warrant any further attention at present

An editorial²⁶ states that an anti-hemorrhagic factor in foods, "a new vitamin-like substance is apparently in process of gradual evolvement". It has antihemorrhagic qualities and is tentatively called vitamin K. This substance is found in association with vitamin C (cevitamic acid) and can be separated from it. It can also be obtained in rather large amounts from alfalfa.

As yet there has not been found any real correlation to hemorrhagic diseases in man. The deficient functioning of the thrombocytes in hemophilia was pointed out by Howell and Cekada, supplementary to Howell's earlier theory regarding the rôle of prothrombia in blood clotting "In vitamin K avitaminosis it is prothrombin that is virtually absent, and the

possible relationship between the two is of considerable interest "

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FOOD POISONING

By Thomas A Johnson, M D

Although the recent literature on food poisoning stresses the bacteriologic etiology of most outbreaks, in individual cases, consideration must be given to other possibilities, such as the ingestion of plants and animals inherently poisonous and the addition of mineral or organic poisons to food in the form of sprays and preservatives

J. L Goforth¹ advises against the use of the term "ptomain poisoning" to indicate food poisoning of obscure origin. There is very little evidence that protein degradation products per se are factors in food poisoning. On the contrary, the wide prevalence in various parts of the world of the custom of eating partially decomposed food attests to its relative innocuousness. Most outbreaks of so-called ptomaine poisoning, on further study, prove to be of bacterial origin.

The frequency of food poisoning is debatable. Undoubtedly many isolated cases of food poisoning are overlooked, or at least passed over, because of the relative lack of serious and prolonged symptoms. Many cases of so-called "intestinal influenza," lasting 12 to 24 hours, on further investigation, might prove to be of toxic or bacterial origin. Specimens of vomitus, diarrhea and suspected food should be investigated bacteriologically in all obscure cases.

Salmonella Food Poisoning

Goforth (loc cit) attributes 70 per cent of the reported outbreaks of food poisoning to organisms of the Salmonella group comprising bacteria of the paratyphoid-enteritides group, of which the most important are B aertrycke, B enteritides (Gartner's) and B surpestifer. (1156)

The toxins give rise to diarrhea, vomiting, and prostration, which, while alarming to the patient, disappear within a few hours without serious sequela Savage² states that the usual course is purely one of gastrointestinal irritation without any circulation of the bacillus in the blood stream The paratyphoid organism is more likely to invade the blood stream giving rise to a true systemic infection W M Frazer, B T J Glover, and V Glass³ report an outbreak of paratyphoid fever with 123 cases and 11 deaths resulting from the ingestion of infected bread handled by a carrier of the B paratyphosum B

E R Jones and H D Wright⁴ reported an outbreak due to B aertrycke, which gained entrance to a milk supply by way of mice excreta. The same author states that rodents frequently are infected with organisms of the Salmonella group

A R Culley quotes Savage and White to the effect that infections of meat with S entertides may occur from three possible primary sources, the ammal, human, or outside contamination

Goforth (*loc cit*) avers that some workers attempt to distinguish between mere absorption of toxins already present in the ingested food and a systemic bacterial infection, on the basis of a short incubation period of two to three hours in the former and one of six to eight hours in the latter. The same author notes that the toxins of *B aertrycke* and *B entertides* are heat resistant and therefore not destroyed by the temperature ordinarily employed to effect sterilization of food. Some strains of the above organisms are more likely to elaborate toxin than others under a variety of condi-

tions The virulence of the organism, the potency of the toxin, the resistance of the patient, and the amount of food ingested all are factors in the individual case Goforth states that the usual manifestations of Salmonella poisoning are nausea, vomiting, cramps, purging, chills, headache, thirst, fever, nervousness, prostration, drowsiness, coma, and occasionally death

Of considerable interest are the European reports of mass poisonings from duck's eggs due to an organism of the paratyphoid group. A group of such cases was reported by E Seligmann, who traced the source of the infection especially to the use of raw duck's eggs in creams, salad dressings, and sauces Comparatively few duck's eggs are used in the United States, however, in individual cases that source should not be overlooked

The treatment of Salmonella food poisoning in man is largely symptomatic together with the rapid elimination of the suspected food, gastric lavage, and supportive measures N Mutch⁷ stresses the value of the administration of *kaolin* because of the wide range of its adsorptive affinities. The administration of *activated charcoal* is said to be of value

P B Matz⁸ discusses the various factors in the institutional control of food poisoning. He concludes that the following are important (1) Personal cleanliness, (2) periodic examination of food handlers, (3) the elimination of flies, rodents, and vernin, and (4) adequate refrigeration.

Staphylococcic Food Poisoning

Poisoning resulting from the ingestion of milk or milk products contaminated with staphylococci has received much attention in the American literature in the past few years. First mentioned by M. A. Barber⁹ and discussed by E. O.

Jordan, 10 the subject has been further clarified in the past seven years. Many workers have confirmed and amplified Jordan's conclusions of 1930, that various strains of staphylococcus of diverse origin and different cultural characters were capable of generating in broth a substance which when taken by mouth produced a gastrointestinal disturbance

C. E Dolman¹¹ suggested that the term, enterotoxin, be applied to that type of staphylococcic toxin responsible for food poisoning. Apparently all staphylococci are not capable of elaborating enterotoxin. G. H. Chapman, C. W. Lieb, and L. Curcio¹² conclude that foodpoisoning strains of staphylococci cannot be differentiated with certainty from other types of staphylococci, although their studies make it possible to approximate the identification. E. O. Jordan and W. Burrows¹³ state that a starchrich medium favors the production of the enterotoxic substance.

The symptomatology of acute staphylococcic enterotoxic poisoning is fairly characteristic according to G. A Denison 14 Nausea develops about two hours after the ingestion of the contaminated food, followed by cramps and vomiting at 5 to 20-minute intervals for one to eight hours Diarrhea occurs either in association with the vomiting or several hours later Occasionally blood is discovered in the stools or vomitus. There is associated shock, headache, and muscle The acute symptoms subside after one to eight hours but generally the patient requires one to two days to Fatalities are rare The temrecover perature in the acute stage is normal or subnormal, but occasionally it rises to 100° F (378° C) Clinically, the condition resembles Salmonella intoxication and can be differentiated only by bacteriologic studies The onset of initial symptoms in Salmonella intoxication is more likely to occur at a later period, generally 12 hours, than the intoxication from staphylococcic enterotoxin.

The incrimination of milk and milk products as sources of enterotoxin has been amply confirmed by many workers, notably Denison (loc cit), Jordan (loc cit.), F C. Kelly and G. M. Dack, ¹⁵ J C. Geiger, A B. Crowley and J. P Gray, ¹⁶ and C E. Dolman ¹⁷ R Gwatkin, S Hadwen and H. M LeGard, ¹⁸ and H J Shaughnessy and T. C Grubb ¹⁹ report staphylococcic enterotoxin arising from mastitis in cows

While the majority of reports of staphylococcic enterotoxic epidemics ascribe the source of the infection to contaminated milk or milk products, other types of food also have been reported, such as ham, tongue, chicken gravy, and chicken salad

Interesting is the report of E O Jordan and W Burrows²⁰ that streptococci, both of the green producing and the hemolytic types can produce a gastroenteric poison similar in its physical characters to the enterotoxic substance produced by staphylococci

J D A Gray,²¹ in reporting a case of food poisoning due to proteus vulgaris, comments on the rarity of that organism as a factor in food poisoning compared to the more frequently encountered staphylococcus and members of the Salmonella group. The symptoms were similar to those encountered in staphylococcus food poisoning, but of somewhat longer duration, *i.e.*, up to 24 to 48 hours.

Botulism

The recent literature contributes very little additional information on the clinical features of botulism, most of the articles dealing with the epidemiology and treatment

Comparing the periods 1918 to 1925 and 1929 to 1935, K F. Meyer²² noted

an increase in the number of reported outbreaks of botulism in the latter period which he attributes to the increased use of the "cold pack" method of preserving food, a method widely used in certain rural districts in the western part of the United States Meyer further comments on the recent rarity of botulism resulting from American commercially canned foods, a factor of safety undubitably related to the uniform adoption of one of the various types of pressure sterilizing

R S Aitken, B Barling, and A. A Mıles²³ report a case of botulısm ın which a prepared minced beef was the source of the toxin Canned meats appear to be incriminated more frequently in European outbreaks of botulism than in the United States, however, Meyer (loc cit) found that canned string beans and corn were the chief offenders in the recorded cases in the United States G G Duncan and O N Smith²⁴ emphasize the necessity of boiling all canned vegetables before serving in order to destroy any botulinus toxin that may be present, a simple precaution which is highly effective due to the ease with which the botulinus toxin is destroyed by heat

Treatment of botulism requires heroic measures Duncan and Smith (loc cit) call attention to the necessity of the early administration of the specific antitoxin All individuals who have partaken of any of the suspected food should receive 10,000 units of the mixed A and B types intramuscularly daily until the specific type has been determined, after which the use of the single type A or B should be continued Treatment begun following the onset of symptoms is much less likely of success J C Geiger²⁵ urges the administration of 10,000 units (50 cc) of the specific antiserum in 1000 cc ten per cent glucose daily F S Caprio²⁶ used 5000 units of mixed A and B antiserum intravenously Geiger (loc. cit.) is impressed with the clinical value of the intravenous administration of ten per cent glucose in cases where the specific antiserum is not available. In view of the paucity of sources of supply in the United States, Duncan and Smith (loc cit) list three depots where botulinus antiserum is available.

- 1 Jensen and Salisbury Lab, Inc, Kansas City, Mo
- 2. Hygiene Laboratory, Washington, D. C.
- 3 Department of Health, New York City.

R B Lindsay, J R Newman, and I. C Hall²⁷ and Duncan and Smith (loc cit) emphasize the value of rest, morphine, liquids, gastric lavage, and opening the bowels as adjuncts in the treatment of botulism

After reviewing the recent literature on bacterial food poisoning, one cannot avoid commenting on the number of cases which were incompletely studied because of the failure on the part of the visiting physician to appreciate the necessity for preserving specimens of suspected food for bacterial examination. The same comment applies to specimens of feces, vomitus and urine. The scope of the present article precludes consideration of the other epidemiologic procedures valuable in determining the various sources of bacterial food contamination.

Toxicity of Fruit Sprays

In certain fruit-growing districts it is customary to spray the fruit-bearing trees with insecticides at periodic intervals. The possibility of food poisoning arising from the ingestion of spray residue, which has been either improperly removed or ignored altogether, has attracted attention recently. J. C. Geiger, G. H. Becker, and A. B. Crowley, 28

commenting on the almost universal use of lead arsenate as a spray, state that no adequate substitute is available W S. Frisbie²⁹ notes the use of "binders" in the form of a caseinate or oil which cause the lead arsenate to adhere more firmly to the fruit. The toxicity of the spray residue has been the subject of much controversy. W F. Cogswell and J. W. Forbes³⁰ report the death of a 15-yearold girl from arsenical poisoning attributed to the ingestion of fruit containing an excess of lead arsenate spray on the surface A J Carlson³¹ believes that the washing of fruit should be sufficient to remove enough lead arsenate to render the fruit safe for human consumption However, Frisbie (loc cit) denies that ordinary washing removes much of the lead-arsenate residue if "binder" has been used. R H Heeren and H. B Funk³² recommend the use of a one per cent hydrochloric acid rinse as an effective means to remove the spray

Frisbie (loc cit) states that for human consumption the Federal authorities limit the amounts of spray residue to 0.01 grain of arsenic trioxide and 0.018 grain of lead per pound of fruit

Nicotine and fluorine have been used as sprays, apparently without any reported instances of food poisoning

Dried Foods

P F Nichols³³ investigated the public health aspects of dried foods. He commented on the paucity of bacteriologic study of dried fruits and vegetables, but nevertheless concluded that the danger of poisoning from pathogenic bacteria was remote. Most drying processes do not result in complete sterilization. The use of lye solution and sulfur (as sulfur dioxide) in the preparation of dried foods offered some toxic possibilities but none have been reported. Nichols comments on the almost complete absence

of recorded cases of food poisoning or infection from dried foods. Nichols noted 52 cases of botulism reported in Russia from the ingestion of salted, fried, or smoked fish, all of which were consumed in the raw state.

Mussel Poisoning

H. Sommer and K F Meyer³⁴ record their observations on the rarely observed poisoning from mussels The exact etiology is still obscure but mussel poisoning in its paralytic form must be distinguished from the allergic type of shellfish poisoning, also from the gastrointestinal form which is caused by spoilage of the mussel or pollution In the paralytic form of mussel poisoning, the symptoms are due to a neuropoison and consist of a tingling sensation in the extremities, followed by numbness, and in severe cases by complete paralysis and death within a few hours. The poison is not counteracted by any known drug Mussel poisoning, occurring chiefly in waters of the northern temperate zone, 15 found in the United States on the western coast only, especially during the summer C H Kellaway,35 using some of the mussel toxin prepared by Sommer (loc cit) reported detailed studies on frogs

In connection with possible advances in the therapy of mushroom poisoning (mycetismus). I. Binet and J. Marek to report their work on experimental animals (dogs and rabbits) which were fed powdered nonedible mushrooms by mouth. The animals developed marked hypoglycemia which responded well to intravenous glucose. The treated animals recovered and the untreated controls died. Furthermore, controls fed with edible mushrooms failed to develop hypoglycemia. Although no comparable studies have been reported in humans,

it is suggested that large amounts of intravenous glucose be administered in the treatment of human mycetismus

Conclusion

E. O Jordan³⁷ states that in a considerable proportion of cases of alleged food poisoning there is a large measure of uncertainty about the real source of trouble, that although the trend of opinion has been in the direction of increased recognition of the share of certain bacteria, there is an important residue of unexplained food poisoning that needs further skilled investigation Jordan further states that the first step is the regular and thorough investigation of every food-poisoning outbreak

Confronted with a case that clinically suggests food-poisoning as a possible etiologic factor, the attending physician should bear in mind certain epidemiologic considerations A careful historical review of the case, not only in respect to recent but to remote food ingestion together with inquiry into the recent health of the family and possibly the patient's associates, may suggest the etioology Of extreme importance is the bacteriological and chemical examinations of vomitus, stools and urine. If the history suggests a particular food, specimens of the food should be sent to the According to J. A. Kolmer laboratory and F Boerner35 500 to 2000 cc of urine and 100 to 200 grams of feces usually are sufficient for complete bacteriological and toxicological examina-The literature is replete with instances illustrating the unfortunate consequences of neglect of the latter precaution In defense of the attending physıcıan, undoubtedly many cases of food poisoning, at least in their incipiency, are of such a mild character that an extensive study does not seem warranted and in some instances the financial status of the patient precludes any but the most urgent laboratory examinations

Treatment of food poisoning varies with the etiologic agent. Certain general principles deserve emphasis Immediate gastric lavage should be employed if there is any possibility that the stomach contains any residue of the suspected food The use of salines and enemas to empty the colon should be considered In many cases it may be necessary to interdict mouth feeding, if so, parenteral fluids may be required Usually, however, the patient can tolerate liquid nourishment The diet should be built up as the general condition of the patient warrants Insofar as many food poisonings are gastrointestinal irritants, the use of some form of bismuth or chalk by mouth is advisable. Adsorbents, such as kaolin or charcoal are of value Antispasmodic medication with one of the atropin series together with some mild sedation are routine Specific therapy, such as antiserum is of paramount importance in certain intoxications of bacteriological origin, such as botulism (loc cit)

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